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보건학 석사 학위논문

Gastric Surgical Site Infection

Risk Prediction Model

위 수술 부위 감염에 위험 예측 모델

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Gastric Surgical Site Infection

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Abstract

Background: Surgical site infections (SSIs) remain a common complication after an operation. Although most SSI can be treated by antibiotics, yet it has been shown to decrease health-related quality of life, increase the risk of readmission, and increase the costs of health care as well. Thus, we need to seek to wipe out or maintain its incidence rate as low as possible. As the strategies to make it happens, understanding the epidemiology and providing surgeons with appropriate risk factors become necessary.

Aim: Developed risk prediction model defining the patient with the high risk of pathogens infection in patients undergoing gastric surgery.

Methods: 4290 participants who underwent gastric surgery from July 2007 to December 2009 that successfully recorded and registered in KONIS, Korean Nosocomial Infections Surveillance System, were analyzed using lasso method to predict the emersion of SSI. Cross validation were applied in order to get tuning parameter value used in lasso process.

Results: Age, sex, NNIS Risk Index, multiple procedures in the same operation, re-operation at the same site, emergency, BMI, diabetes, as well as current smoking status were statistically significant

factors for SSI after gastric surgery. Among them, re-operation was a factor that gave the largest contribution on the emergence of SSI with the probability alone about 0.14 or 8.8 times higher risk compared to non re-operation; followed by multiple procedures with probability 0.034. If high risk is defined as the probability larger than or equal to 0.33, thus when these both criteria were met, the risk would increase with probability about 0.20 which made the presence of re-operation and multiple procedures at once a kind of high-risk warning of getting infected after surgery. Moreover, when other additional factors were combined, the resulting risk would be even higher, with value in the range of 0.20 - 0.81. In terms of BMI, patients with $BMI < 18.5$ or $25 \leq BMI < 30$ showed no significant difference risk but patient with $BMI \geq 30$ had higher risk as much as 25% compared to them who under/overweight.

Conclusion: Model building based on lasso problem is better than stepwise logistic regression and can produce a good and well calibrated risk prediction model on gastric SSI. This study shows that the emersion of gastric SSI is more affected by environmental/treatment factors, especially re-operation and multiple procedures, rather than host factors. Therefore, the surgeons are expected to be more careful in patient selection, preparation and medical care provision.

Keywords: SSI, gastric surgery, KONIS, lasso, cross validation

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Contents

| | |
|--|-------------|
| Abstract | i |
| List of Tables | v |
| List of Figures | vi |
| List of Abbreviations | viii |
| Chapter 1. Introduction | 1 |
| 제 1 절 Background | 1 |
| 제 2 절 Scope of Study | 3 |
| 제 3 절 Objective | 3 |
| Chapter 2. Data and Methods | 4 |
| 제 1 절 Study Participants | 4 |
| 제 2 절 NNIS Risk Index Measurements | 5 |
| 제 3 절 Statistical Methods | 5 |
| 제 3.1 절 Definition of Lasso | 7 |
| 제 3.2 절 Geometry of Lasso | 8 |
| 제 3.3 절 Prediction Error and Estimation of Tuning Parameter by k -Fold Cross Validation | 10 |
| Chapter 3. Results | 12 |
| 제 1 절 Study Participants | 12 |
| 제 2 절 Basic Description | 13 |
| 제 3 절 Multicollinearity Diagnostic | 16 |
| 제 4 절 Lasso-Prediction Model | 18 |

| | |
|---------------------------------|----|
| Chapter 4. Discussion | 38 |
| References | 41 |
| Appendix | 46 |
| Abstract in Korean (국문초록) | 62 |

List of Tables

| | | |
|--------------------|--|----|
| [Table 3-1] | Basic Characteristics | 14 |
| [Table 3-2] | Multicollinearity Diagnostic (intercept adjusted) | 17 |
| [Table 3-3] | Estimate Beta Coefficients of Model A and Model B | 25 |
| [Table 3-4] | Hosmer-Lemeshow Goodness of Fit Test of Model A (fitted on testing data set) | 29 |
| [Table 3-5] | Hosmer-Lemeshow Goodness of Fit Test of Model B (fitted on testing data set) | 32 |
| [Table 3-6] | Conversion table of lasso estimation to probability of getting infection after gastric surgery | 34 |
| [Table 3-7] | Estimate risk of gastric SSI by simple combination of risk factors in which multiple procedures and re-operation considered as fixed risk factors | 36 |
| [Appendix Table 1] | Details combination of risk factors classified as having high probability of gastric SSI | 46 |

List of Figures

| | | |
|--------------|---|----|
| [Figure 2.1] | Estimation Picture of Lasso and Ridge Regression... | 9 |
| [Figure 2.2] | Comparison of Squared Bias, Variance, and Test MSE Plots for the Lasso Model | 11 |
| [Figure 3.1] | Distribution of Age | 13 |
| [Figure 3.2] | Beta-Lasso Coefficients' Flow Chart..... | 18 |
| [Figure 3.3] | AUC by Bolasso Concept | 20 |
| [Figure 3.4] | Scheme of Model Selection | 21 |
| [Figure 3.5] | Lasso Coefficients on Model A as a Function of λ | 23 |
| [Figure 3.6] | Lasso Coefficients on Model B as a Function of λ | 24 |
| [Figure 3.7] | Cross-validation curve of Model A with upper and lower standard deviation along the λ sequence..... | 26 |
| [Figure 3.8] | Cross-validation curve of Model B with upper and lower standard deviation along the λ sequence..... | 27 |
| [Figure 3.9] | AUC of Model A Fitted on Testing Data Set ... | 28 |

| | |
|--|----|
| [Figure 3.10] Calibration Plot of Model A Fitted on Testing Data Set | 28 |
| [Figure 3.11] AUC of Model B: fitted on training and testing set | 30 |
| [Figure 3.12] Calibration Plot of Model B: fitted on training and testing set | 31 |
| [Figure 3.13] AUC of Model A by Stepwise Logistic Regression | 33 |
| [Figure 3.14] AUC of Model B by Stepwise Logistic Regression | 33 |

List of Abbreviations

| | |
|--------------|--|
| ASA | : American Society of Anesthesiologists |
| AUC | : Area Under Curve |
| BMI | : Body Mass Index |
| BSI | : Bloodstream Infections |
| CDC | : Centers for Disease Control and Prevention |
| CV | : Cross Validation |
| KONIS | : Korean Nosocomial Infections Surveillance System |
| Lasso | : Least Absolute Shrinkage and Selection Operator |
| MSE | : Mean-Squared Error |
| NHSN | : National Healthcare Safety Network |
| NNIS | : National Nosocomial Infections Surveillance |
| OLS | : Ordinary Least Squares |
| PNEU | : Pneumonia |
| SSI | : Surgical Site Infections |
| UTI | : Urinary Tract Infections |

I. Introduction

1. Background

Infection, the entry and development or multiplication of an infectious agent within the body¹, may either cause no symptoms and be subclinical or may cause symptoms and be clinically evident. Infections that occur in the wound spawned by a surgical procedure giving rise to local signs and symptoms, such as heat, redness, pain and swelling, and in more serious cases with systemic signs of fever or a raised white blood cell count could be referred to as surgical site infections (SSIs)². SSI remains a common complication after an operation. The majority of SSIs become noticeable within 30 days of an operative procedure and most often between the fifth and tenth postoperative days². Among surgical patients, SSIs account for 38% of health-care-associated infections³. In Korea, its incidence rate ranges from 2.0% to 9.7%⁴⁻⁷.

Conventionally, SSI rates calculated by the Centers for Disease Control and Prevention (CDC) and other National Healthcare Safety Network (NHSN) have been stratified using a National Nosocomial Infections Surveillance (NNIS) risk index of three equally weighted factors: the American Society of Anesthesiologists (ASA) score, wound classification, and duration of operative procedure⁸⁻¹⁰. ASA score is a subjective assessment that evaluates the overall

physical health status of patients before surgery which is based on five classes (1 – 5): a completely healthy patient; a patient with mild systemic disease; a patient with severe systemic disease; a patient with severe systemic disease that is a constant threat to life; and a moribund patient who is not expected to survive 24 hour with or without surgery¹¹. The wound classification, an assessment of the level of contamination of the surgical wound, developed by the National Academy of Sciences in the 1960s classified into four levels of risk: clean; clean-contaminated; contaminated; and dirty or infected². While duration of operative procedure is measured by calculating T-Hour, whether or not T time is approximate the 75th percentile of the distribution of operation time for a specific procedures category, rounded to the nearest hour¹².

Nowadays, many studies build new model incorporates the 3 NHSN risk index variables and additional data elements, such as alcohol¹³; diabetes, smoking^{13,14}; obesity^{13,15}; BMI¹⁶; general anesthesia^{17,18}; trauma¹⁸; emergency surgery (unscheduled operative procedure), endoscopy^{18,19}. These additional variables based on studies of various surgical procedures including gastrointestinal, orthopedic, gynecologic, cardiac surgery, abdominal hysterectomy, hip-knee arthroplasty and others.

Although most SSI can be treated by antibiotics, yet it has been shown to decrease health-related quality of life, increase the risk of readmission, prolong the length of hospital stay and thereby increase the costs of health care²⁰. Therefore, we need to wipe out

SSI or try to keep its incidence rate as low as possible. As the keys in strategies to reduce SSI incidence rate, understanding the epidemiology and providing surgeons with appropriate risk factors of SSI become more important.

2. Scope of Study

Among many surgical types, it seems that gastrointestinal surgery is relatively common in Korea especially for treatment of gastric cancer. Based on the 2007 National Survey in Korea, gastric cancer incidence rate in men and women respectively were 62.8 and 25.7 cases per 100,000 people²¹. While currently, there is still little information available on risk factors for SSIs after gastrectomy²², thus in this study, the scope is limited only for gastric surgery.

3. Objective

The aim of this study is to develop risk prediction model defining the patients with high risk of pathogens infection in patient undergoing gastric surgery. From this model we will be able to find variables that have more effects and mainly associate with gastric SSI so that we can help surgeons to design an intervention to control or reduce gastric surgical site infection incidence rate.

II. Data and Methods

1. Study Participants

The data were collected by Korean Nosocomial Infections Surveillance System (KONIS). KONIS was founded on November 15th 1995 with purposes to identify nationwide hospital related infection rate by analyzing surveillance data on regular basis and to reduce the rate of device-associated infections as well²³. Started with 15 general hospitals in 1995, the number of hospital registered in the system accrued became 81 hospitals in 2011 - 2012, which scattered in various areas: 26 hospitals in Seoul, 24 hospitals in Kangwon/ Gyeonggi/ Incheon, and 31 hospitals in Central/ South²⁴. Types of data collected by KONIS include urinary tract infections (UTI), bloodstream infections (BSI), pneumonia (PNEU), and 15 surgical procedures including gastric surgery²⁴.

17,421 patients from 39 hospitals from July 2007 to December 2012 underwent gastric surgery. Since most SSIs are noticeable within 30 days post operation, thus this study only focused on SSIs within 30 days post surgical procedures and any infections occurred after 30 postoperative days will be excluded. In the analyzing process, the dependent variable would be gastric surgical site infection. While the independent variables were age, sex, NNIS risk index, general anesthesia, multiple procedures in the same operation, re-operation,

trauma, emergency, endoscopy/laparoscopy, BMI, diabetes, and current smoking status.

2. NNIS Risk Index Measurements

Participants underwent surgery were all measured for ASA score, wound type and length of operation as well. NNIS risk index which developed by CDC in 1991²⁵, has 4 classes which ranges from 0 to 3 points. One point is given for each of the following when commenced:

- ASA score more than 2,
- Either contaminated or dirty/infected wound classification, and
- Length of operation exceeds T-hour¹².

3. Statistical Methods

In order to quantitatively describe the main information of a collection of data, including analysis of frequency data, the chi-square test was used. Chi-square was chosen since all available parameters converted into categorical variables.

Suppose we have n independent observations, response y , and p parameters; then the linear model postulates

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p + \varepsilon \quad (2.1)$$

for an error ε with mean 0. The model is convenient for

predictions where the idea is that the system under study is approximately linear and we are interested in estimating the coefficient $\beta_i, i=0, \dots, p$. Ordinary least squares (OLS) is one of the estimation methods for estimating the unknown parameter by minimizing the residual squared error. However, sometimes we just not satisfied with OLS estimates since often have low bias but large variance which affect the prediction accuracy as well as difficult to interpret, especially if we work with a large number of parameters, so that we would like to determine smaller subset that displays the strongest effect²⁶.

To improve prediction accuracy, we can set some coefficients into 0 (shrinking); although by doing it will sacrifice little bias, yet it can reduce the variance of the predicted values and therefore increase the overall prediction accuracy²⁶. Ridge regression shrinks the regression coefficients by impelling a penalty on their size and the ridge coefficients minimize a penalized residual sum of squares,

$$\hat{\beta}^{ridge} = \arg \min_{\beta} \left\{ \sum_{i=1}^n (y_i - \beta_0 - \sum_{j=1}^p \beta_j x_{ij})^2 + \lambda \sum_{j=1}^p \beta_j^2 \right\} \quad (2.2)$$

with $\lambda \geq 0$, is a peculiarity parameter that controls the amount of shrinkage²⁷. Although ridge regression is a process that shrinks coefficient and hence more stable: yet it does not set any coefficients to 0, therefore it does not give an easy interpretable model²⁶. Thus, in order to make prediction model in gastric surgical site infections, the technique called Lasso (least

absolute shrinkage and selection operator) which proposed by Tibshirani in 1994 was used. This method shrinks some coefficients and set others to 0.

Not only suitable for variable selection, Lasso also can handle multicollinearity that exists among variables. Multicollinearity may increase the standard errors of the coefficients which will make some statistically significant variables become insignificant. The investigation of multicollinearity is examined by calculating the kappa value as well as determinant of covariance matrix which later was emphasized by proportion of variation score among variables with cut off point 0.5.

All the computation works in this study were done using SAS version 9.3 and R version i386 3.1.0 software. Specifically, basic descriptive statistics and multicollinearity analysis were done by SAS while the whole lasso procedures, including cross validation, were processed by R.

3.1. Definition of Lasso

Suppose we have n independent observations and p predictors, that is $(x^i, y_i), i = 1, 2, \dots, n$ where $x^i = (x_{i1}, \dots, x_{ip})^T$ are the predictor variables and y_i are the responses. Assumed that x_{ij} are standardized so that $\sum_i \frac{x_{ij}}{n} = 0, \sum_i \frac{x_{ij}^2}{n} = 1$. Let $\hat{\beta} = (\hat{\beta}_1, \dots, \hat{\beta}_p)$, the lasso estimate $\hat{\beta}$ (Tibshirani, 1996) is defined by

$$\hat{\beta}^{lasso} = \arg \min_{\beta} \left\{ \sum_{i=1}^n (y_i - \beta_0 - \sum_{j=1}^p \beta_j x_{ij})^2 \right\} \text{ subject to } \sum_{j=1}^p |\beta_j| \leq t \quad (2.3)$$

where $t \geq 0$ is a tuning parameter and $\forall t$, the estimator of β_0 is $\hat{\beta}_0 = \bar{y}$. Let β_j^o be the full least squares estimates and let $t_0 = \sum |\hat{\beta}_j^o|$, by making t adequately small, $t < t_0$, will cause some of the coefficients to be exactly equal to 0. Equation (2.3) could also be written in the equivalent of Lagrangian form (Hastie T, et al, 2008) as

$$\hat{\beta}^{lasso} = \arg \min_{\beta} \left\{ \sum_{i=1}^n (y_i - \beta_0 - \sum_{j=1}^p \beta_j x_{ij})^2 + \lambda \sum_{j=1}^p |\beta_j| \right\} \quad (2.4)$$

when λ increases, more coefficients are set to 0, leading to less variables are selected. From equation (2.2) and (2.4), we can remark the similarity of lasso and ridge regression model. However, only the penalty function is different: the L2 ridge penalty $\sum_{j=1}^p \beta_j^2$ is changed by L1 lasso penalty $\sum_{j=1}^p |\beta_j|$. The change in the penalty function is delicate yet gives a dramatic effect on the resulting estimator.

3.2. Geometry of Lasso

Let \mathbf{X} be $n \times p$ matrix with x_{ij} elements, and $\mathbf{X}^T \mathbf{X} = \mathbf{I}$, the identity matrix. Suppose we have 2 predictors, $p=2$, the criterion (Tibshirani, 1996):

$$\sum_{i=1}^n (y_i - \sum_j \beta_j x_{ij})^2 = (\beta - \hat{\beta}^o)^T \mathbf{X}^T \mathbf{X} (\beta - \hat{\beta}^o) + (\text{Constant}) \quad (2.5)$$

The elliptical contours of the least square errors function are shown by the red ellipses curves in Figure 2.1 which are centered at the OLS estimates, while the solid blue areas are the constraint region, respectively $|\beta_1| + |\beta_2| \leq t$ and $\beta_1^2 + \beta_2^2 \leq t^2$

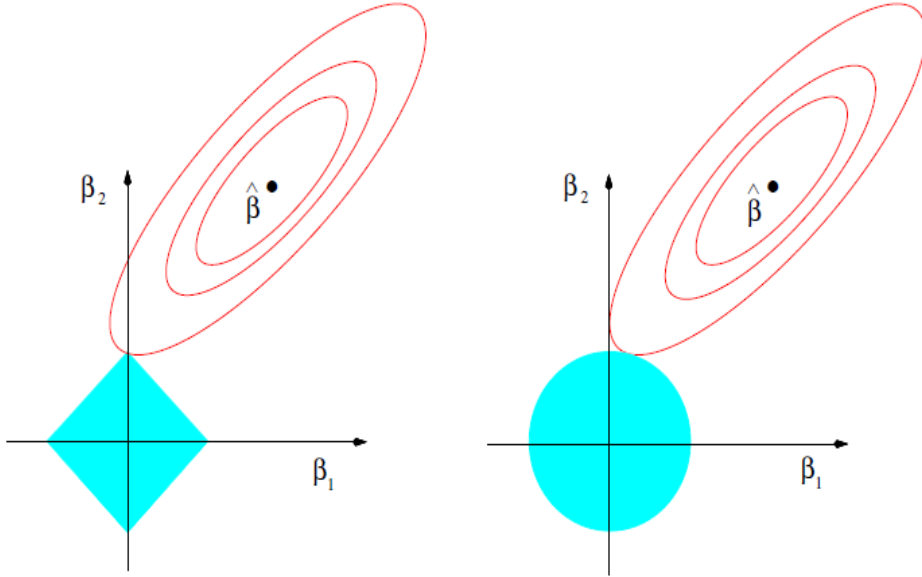


Figure 2.1. Estimation Picture of Lasso (left) and Ridge Regression (right). (Hastie Trevor et. al, 2008)

The lasso solution is the first place that the contours touch the diamond, this may sometimes occurs at a corner which leads to a zero coefficient (Fig. 2.1 (left)). On the contrary, we cannot do this with ridge regression (Fig. 2.1 (right)), since it is circle, there are no corner for the contours to hit, thus zero coefficients will rarely obtained²⁶.

3.3. Prediction Error and Estimation of Tuning Parameter by k -Fold Cross Validation

To determine the best model by applying lasso requires the best value of tuning parameter t in (2.3) or λ in (2.4), and one of the methods that provides simple way for handling and selecting the value is by implementing cross-validation. This approach is randomly dividing the set of observations into k approximately equal size-groups (k -fold CV). The first fold is treated as a validation set which later on fitted on the remaining $k - 1$ folds and the mean-squared error, MSE, is calculated afterwards²⁸.

Assumed the (X, Y) observations are drawn from unknown distribution; 'X-random' case. Let $Y = \eta(X) + \varepsilon$ where $E[\varepsilon] = 0$ and $\text{var}(\varepsilon) = \sigma^2$. The mean-squared error of an estimate $\hat{\eta}(X)$ is obtained by

$$MSE = E[\hat{\eta}(X) - \eta(X)]^2 \quad (2.6)$$

the expected value taken over the joint distribution of X and Y with fixed $\hat{\eta}(X)$ ²⁶.

The procedure is repeated for k times; each time, different group of observations is treated as a validation set. Resulting in k estimates of the test error, we will have $MSE_1, MSE_2, \dots, MSE_k$ and the k -fold cross validation estimation is calculated by taking the average over k folds:

$$CV_{(k)} = \frac{1}{k} \sum_{i=1}^k MSE_i \quad (2.7)$$

thus when used for selecting tuning parameter, CV is applied with

different values and we select the location that yields the minimum point in the estimated of CV error. The model then is re-fitted using all observations data and the selected value of tuning parameter²⁸.

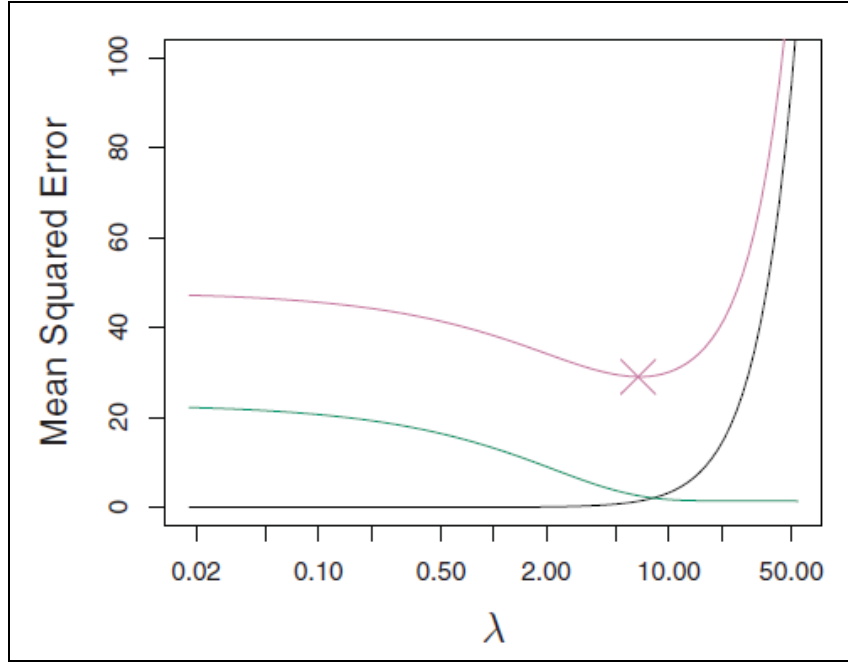


Figure 2.2. Comparison of Squared Bias (black), Variance (green), and Test MSE (purple) Plots for the Lasso Model
(James Gareth et. al, 2013)

The number k of folds is important parameters of the tuning process²⁹. Performing large k folds of CV will definitely take more time; therefore in this study, by setting $k = 10$ would make it more feasible.

III. Results

1. Study Participants

Out of 17,421 participants who underwent gastric surgery recorded from July 2007 to December 2012; 13,124 data from 2010 to 2012 were excluded due to lack of information on BMI, diabetes, and current smoking status variables, whereas these 3 parameters are statistically significant factors contributing to SSI^{13,30,31}. Additionally, 6 infection cases were omitted since occurred after 30 days postoperative while 1 case was excluded due to missing information on NNIS risk score; hence in total, number of sample size that studied and analyzed for gastric SSI was 4290 participants.

As all participants underwent operation with general anesthesia procedure, hence variable "general anesthesia" was excluded from analysis process. The same thing was done for variable "trauma", as only 6 patients with trauma yet no indication of infection post surgery, thus this variable was eliminated from analysis since it could hide the real effect of trauma (underestimate the true trauma effect to the occurrence of SSI), when there is an evidence that trauma can increase the risk of infection¹⁸.

2. Basic Description

Among 4290 participants, 164 people of them got infected post gastric operation. In general, median of age was reported at 60 year; 58 for female and 61 for male in particular. The age distribution can be seen in Figure 3.1. Meanwhile, based on the analysis using chi-square, male had higher risk of getting SSI compared to female with relative risk 2.06. Higher NNIS risk score proportionate with higher risk of getting infected after operation. Moreover, re-operation; emergency operative procedure; multiple procedures in the same operation; diabetes; as well as current smoking status were statistically significant for $\alpha=0.05$. Among statistically significant factors of gastric SSI, re-operation seemed had the strongest effect. Patient who underwent re-operation at the same site had 7 times higher risk than patients who did not get re-operation. The details information on basic characteristics of the study participants is shown in Table 3.1.

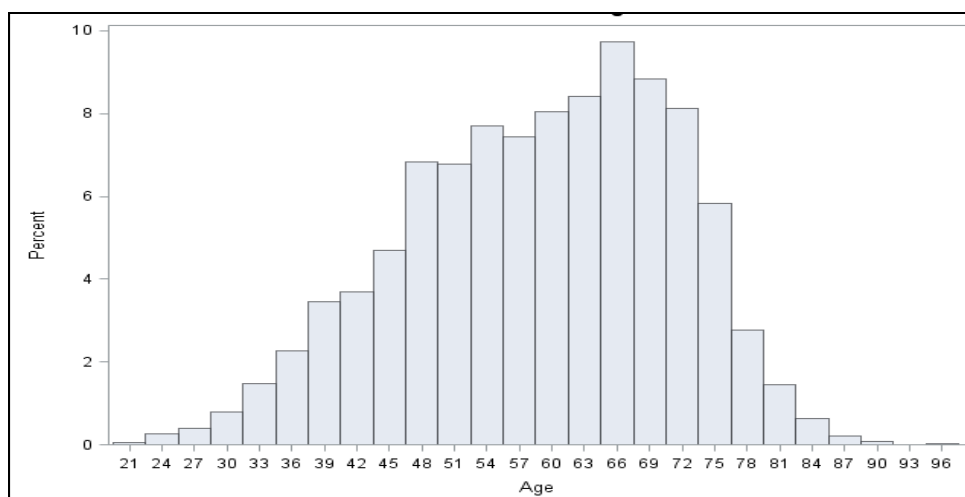


Figure 3.1. Distribution of Age

Table 3.1. Basic Characteristics

| Characteristics | Total | Without SSI | | With SSI | | p-value |
|--|-------------|-------------|--------|----------|--------|------------------|
| | | (n) | (%) | (n) | (%) | |
| Sex | 4290 | | | | | <.0001 |
| Female | 1500 | 1466 | 97.73% | 34 | 2.27% | |
| Male | 2790 | 2660 | 95.34% | 130 | 4.66% | |
| Age at Operation | 4290 | | | | | 0.1243 |
| 21 ≤ Age ≤ 35 | 161 | 158 | 98.14% | 3 | 1.86% | |
| 36 ≤ Age ≤ 50 | 956 | 929 | 97.18% | 27 | 2.82% | |
| 51 ≤ Age ≤ 65 | 1689 | 1616 | 95.68% | 73 | 4.32% | |
| Age > 65 | 1484 | 1423 | 95.89% | 61 | 4.11% | |
| NNIS Risk Index | 4290 | | | | | <.0001 |
| 0 | 2995 | 2908 | 97.10% | 87 | 2.90% | |
| 1 | 1196 | 1127 | 94.23% | 69 | 5.77% | |
| 2 | 99 | 91 | 91.92% | 8 | 8.08% | |
| Re-operation (on the same site) | 4290 | | | | | <.0001 |
| No | 4217 | 4072 | 96.56% | 145 | 3.44% | |
| Yes | 73 | 54 | 73.97% | 19 | 26.03% | |
| Emergency Operative Procedure | 4290 | | | | | 0.0005 |
| No | 4178 | 4026 | 96.36% | 152 | 3.64% | |
| Yes | 112 | 100 | 89.29% | 12 | 10.71% | |

Table 3.1. (continue) Basic Characteristics

| Characteristics | Total | Without SSI | | With SSI | | p-value |
|-----------------------------------|-------------|-------------|--------|----------|-------|------------------|
| | | (n) | (%) | (n) | (%) | |
| Multiple Procedures | 4290 | | | | | <.0001 |
| No | 3836 | 3710 | 96.72% | 126 | 3.28% | |
| Yes | 454 | 416 | 91.63% | 38 | 8.37% | |
| DM | 4290 | | | | | 0.0024 |
| No | 3735 | 3605 | 96.52% | 130 | 3.48% | |
| Yes | 555 | 521 | 93.87% | 34 | 6.13% | |
| Smoking Status | 4290 | | | | | 0.0077 |
| No | 3322 | 3209 | 96.60% | 113 | 3.40% | |
| Yes | 968 | 917 | 94.73% | 51 | 5.27% | |
| Endoscopy/ Laparoscopy | 4290 | | | | | 0.0685 |
| No | 3023 | 2897 | 95.83% | 126 | 4.17% | |
| Yes | 1267 | 1229 | 97.00% | 38 | 3.00% | |
| BMI | 4290 | | | | | 0.2888 |
| BMI < 18.5 | 288 | 275 | 95.49% | 13 | 4.51% | |
| 18.5 ≤ BMI < 25 | 2807 | 2711 | 96.58% | 96 | 3.42% | |
| 25 ≤ BMI < 30 | 1082 | 1033 | 95.47% | 49 | 4.53% | |
| BMI ≥ 30 | 113 | 107 | 94.69% | 6 | 5.31% | |

3. Multicollinearity Diagnostic

When making a model, we look at the correlation between predictors and a response. In regression analysis, before inputting every potential predictor under study into the model, we better to investigate the presence of multicollinearity. It occurs when two or more predictors are highly correlated (proportion of variation larger than 0.50).

The presence of multicollinearity can also be analyzed by kappa value. In this study the kappa value, $\kappa = 8.9646 < 10$ which indicated reasonable correlation. However, the determinant value of covariance matrix was very small with $3.476189\text{E-}14$, indicated perfect co-linearity. The result also supported by Table 3.2 that showed us the possibility of multicollinearity between obesity and male sex; also smoking and BMI with proportion of variation, respectively, 0.591 for obesity and male sex; while 0.919 - 0.908 - 0.603 for smoking and BMI (normal - overweight - obesity, in particular).

Table 3.2. Multicollinearity Diagnostic (intercept adjusted)

| Number | Proportion of Variation | | | | | | | | | | | | |
|------------------------|-------------------------|-------|-------|--------------|-----------|---------------------|--------------|------------------------|-------|--------------|------------------|-------------|--------------|
| | Age (>50) | NNIS1 | NNIS2 | Male | Emergency | Multiple Procedures | Re-operation | endoscopy/ laparoscopy | DM | BMI (normal) | BMI (overweight) | BMI (Obese) | smoking |
| Age (>50) | 0.001 | 0.001 | 0.001 | 0.001 | 0.005 | 0.001 | 0.000 | 0.006 | 0.006 | 0.070 | 0.068 | 0.007 | 0.003 |
| NNIS1 | 0.052 | 0.017 | 0.079 | 0.162 | 0.077 | 0.031 | 0.019 | 0.055 | 0.017 | 0.001 | 0.003 | 0.014 | 0.088 |
| NNIS2 | 0.032 | 0.003 | 0.117 | 0.126 | 0.103 | 0.058 | 0.056 | 0.000 | 0.006 | 0.000 | 0.001 | 0.009 | 0.209 |
| Male | 0.039 | 0.341 | 0.123 | 0.000 | 0.063 | 0.153 | 0.011 | 0.002 | 0.058 | 0.001 | 0.001 | 0.000 | 0.011 |
| Emergency | 0.278 | 0.096 | 0.005 | 0.000 | 0.055 | 0.055 | 0.069 | 0.018 | 0.087 | 0.002 | 0.001 | 0.091 | 0.047 |
| Multiple Procedures | 0.020 | 0.000 | 0.006 | 0.015 | 0.002 | 0.065 | 0.001 | 0.121 | 0.265 | 0.000 | 0.013 | 0.250 | 0.017 |
| Re-operation | 0.001 | 0.019 | 0.065 | 0.000 | 0.003 | 0.105 | 0.480 | 0.115 | 0.027 | 0.002 | 0.002 | 0.120 | 0.001 |
| endoscopy/ laparoscopy | 0.005 | 0.014 | 0.062 | 0.001 | 0.025 | 0.034 | 0.201 | 0.539 | 0.001 | 0.002 | 0.002 | 0.107 | 0.002 |
| DM | 0.264 | 0.115 | 0.013 | 0.021 | 0.054 | 0.162 | 0.019 | 0.007 | 0.408 | 0.001 | 0.001 | 0.022 | 0.016 |
| BMI (normal) | 0.079 | 0.079 | 0.033 | 0.070 | 0.322 | 0.156 | 0.135 | 0.112 | 0.111 | 0.000 | 0.001 | 0.020 | 0.000 |
| BMI (overweight) | 0.047 | 0.315 | 0.496 | 0.013 | 0.286 | 0.173 | 0.003 | 0.019 | 0.001 | 0.001 | 0.000 | 0.002 | 0.000 |
| BMI (Obese) | 0.177 | 0.000 | 0.000 | 0.591 | 0.002 | 0.007 | 0.003 | 0.002 | 0.009 | 0.000 | 0.000 | 0.000 | 0.603 |
| smoking | 0.004 | 0.000 | 0.000 | 0.001 | 0.002 | 0.002 | 0.002 | 0.004 | 0.006 | 0.919 | 0.908 | 0.357 | 0.002 |

Note: Cell with bold ink and grey highlight color are pair of variables with proportion of variation > 0.50 indicated possibility of high correlation among them

4. Lasso-Prediction Model

As the presence of multicollinearity was detected in the data, hence the method for prediction model would be built based on lasso problem. The following Figure 3.2 is the scheme in obtaining lasso estimation of gastric SSI's risk factors.

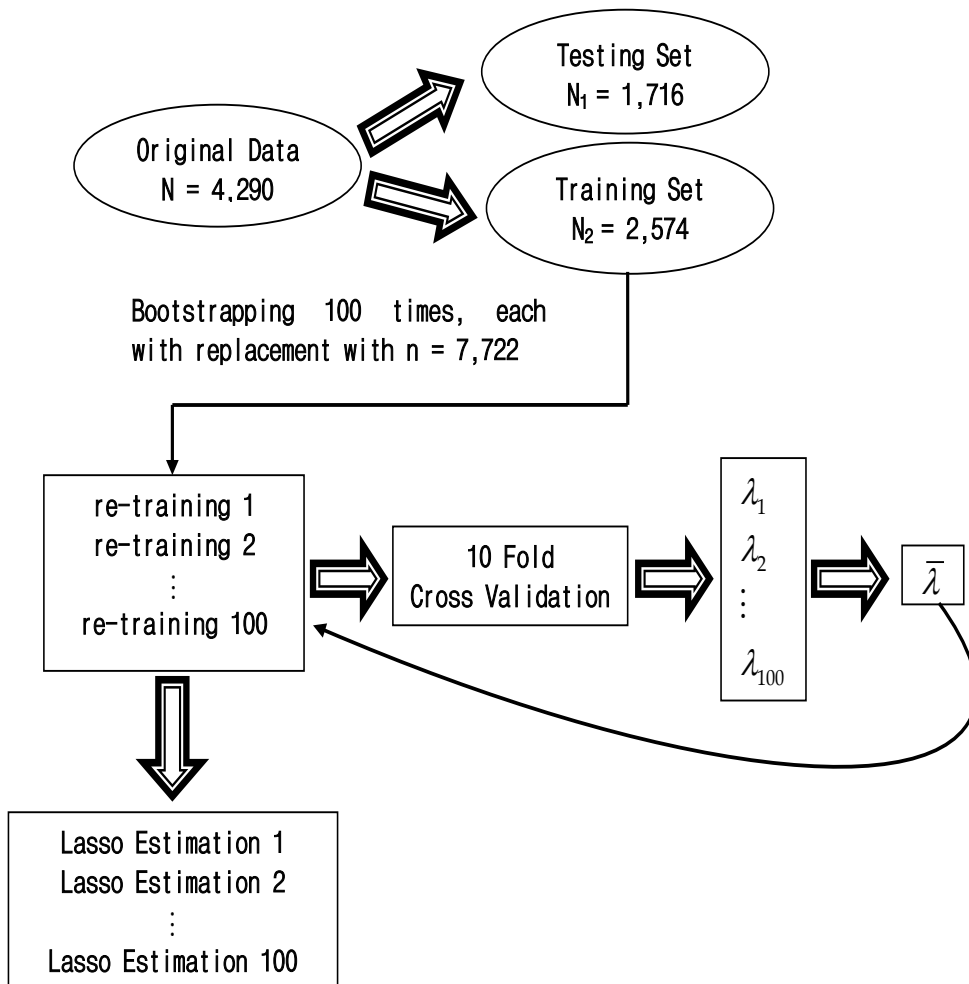


Figure 3.2. Beta-Lasso Coefficients' Flow Chart

The data was randomly divided into testing and training set with proportion 40% and 60% respectively. In order to obtain more stable results, 100 re-training set were bootstrapped with size 3 times higher than the original training data. All re-training set would be used to build up a model to predict response value based on 10 predictors.

100 tuning parameter values, $\lambda_i, i \in \{1, 2, \dots, 100\}$ were obtained by applying 10-fold cross validation into each re-training set. Furthermore, from 100 lambda values, the average lambda, $\bar{\lambda}$, was later on fitted into each re-training set in order to get 100 subsets of variables. The average lambda was chosen as the best lambda since it gave better and stable results compared to using each lambda values when re-fitted into testing set. From the analysis, we obtained

$$\bar{\lambda} = 0.0007802577; \log(\bar{\lambda}) = -7.155886$$

which gave mean, median, and mode of c-statistics over 100 models performance, respectively were 0.710; 0.712; and 0.717 compare to 0.699; 0.700; and 0.693 when used lambda from cross validation of each re-training set.

As 100 subsets of variables with its each estimate value were obtained; in terms of model performances (AUC, Brier Score, Hosmer-Lemeshow, and calibration plot), which one should be chosen to get the best of estimate beta coefficients that would give the best prediction of gastric SSI?

Francis R. Bach proposed Bolasso (Bootstrapped Lasso) in 2008 which believed gave more consistent lasso estimation. In Bolasso concept, we suppose to generate bootstrap samples for k times, then compute lasso estimate of $\hat{\beta}_j^k$ from $(X^k, Y^k) \in \mathbb{R}^{n \times (p+1)}$ and $J_k = \{j, \hat{\beta}_j^k \neq 0\}$ to find $J = \bigcap_k J_k$ which later on used to calculate $\hat{\beta}_j$ from (X_J, Y) ³². Unfortunately, this method seemed not well fitted to be applied in this study, indicated by AUC less than 0.70 (Figure 3.3).

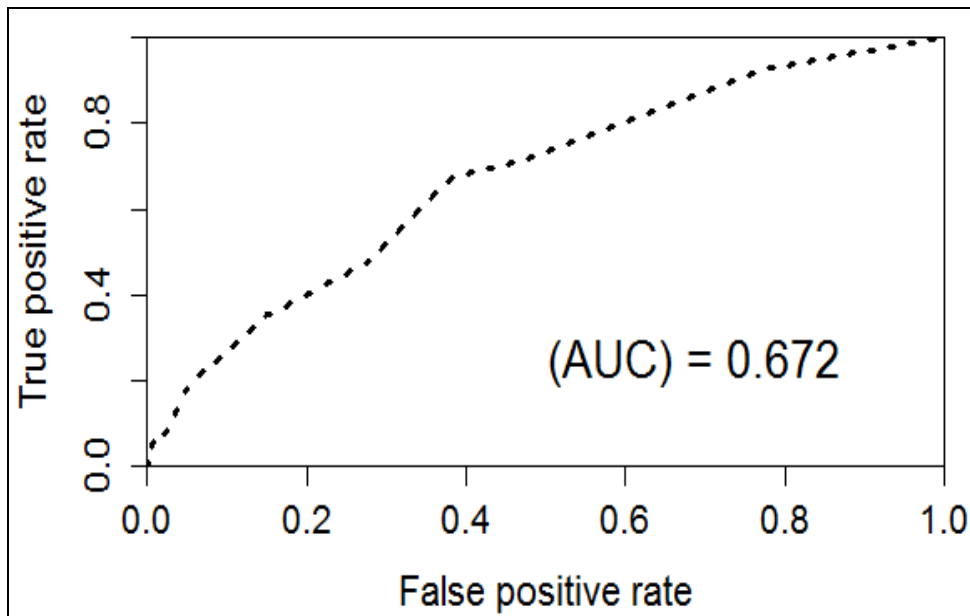


Figure 3.3. AUC by Bolasso Concept

Since all Brier scores were quiet similar, ranges from 0.03544 to 0.03614, with average 0.03569; therefore in finding the best subset of variables, the selection process was done based on AUC and Hosmer-Lemeshow P-value (Figure 3.4).

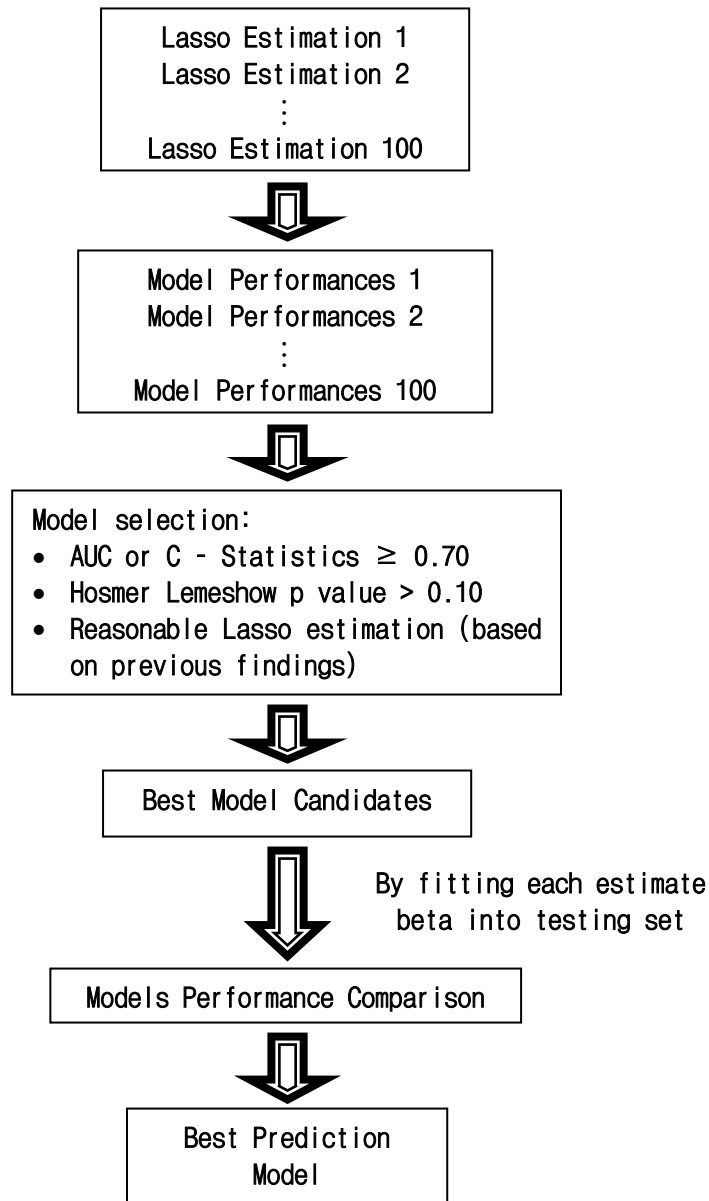


Figure 3.4. Scheme of Model Selection

C-statistics larger than or equal to 0.70 was used as in general, 0.70 is considered as the cut off point to distinguish whether the predictive accuracy is fair or not. While alpha 0.10 was chosen for Hosmer-Lemeshow goodness of fit test because in most cases, a model fits the training set better than it fits the testing set.

Therefore when it fitted into the test set, although the performance would be lower, yet it is expected that the model would also indicate no evidence of poor fit by having p-value larger than 0.05, like most alpha value used in general hypothesis testing. On the other hand, the probability of type I error should be also controlled so that the value would not be too large, thus 0.10 was considered as the best cut off point.

From 100 models, 75 had AUC larger than or equal to 0.70. Among them, 66 were statistically displayed correctly specified, for which expected and observed event rates in subgroups were similar, using $\alpha=0.10$. Hereinafter, 66 beta coefficients subsets corresponding to the selected models were analyzed and only 2 models remained, meanwhile another 64 were excluded due to infelicity of the beta values. For instance, higher NNIS risk index corresponded with lower beta value; whereas, based on reported previous findings, higher NNIS score proportional to higher risk of gastric SSI³³. Another irregularity, such as compared to elective surgery, emergency had lower risk; whereas, having unscheduled operative procedure would increase the risk of getting infection³⁴.

As 2 models remained, namely: model A (AUC = 0.717, Hosmer-Lemeshow p-value = 0.8014, Brier Score = 0.03550) and model B (AUC = 0.723, Hosmer-Lemeshow p-value = 0.8269, Brier Score = 0.03558); therefore in selecting the best subset would be easier. The lasso estimation of both models can be seen in Table 3.3 while the coefficients value at several points of lambda shown in Figure 3.5 – 3.6.

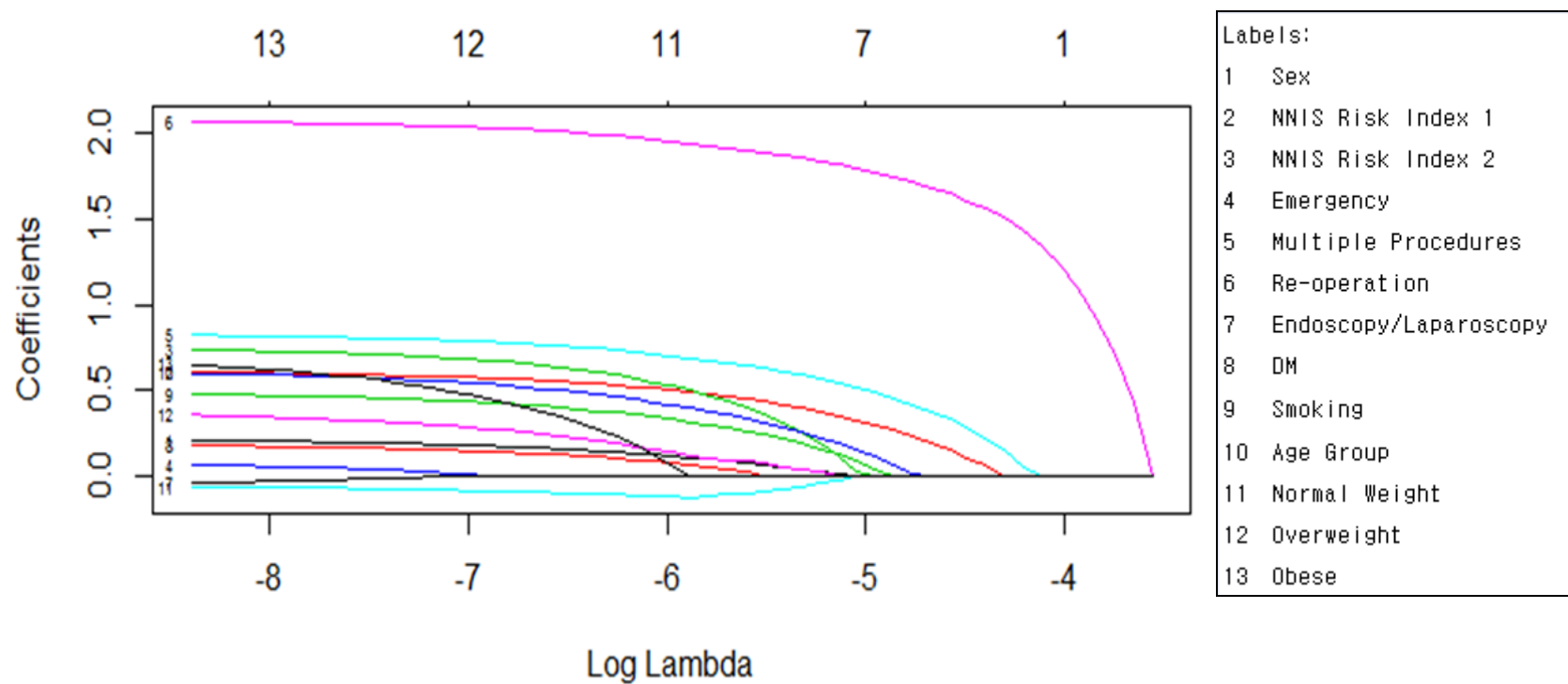


Figure 3.5. Lasso Coefficients on Model A as a Function of λ

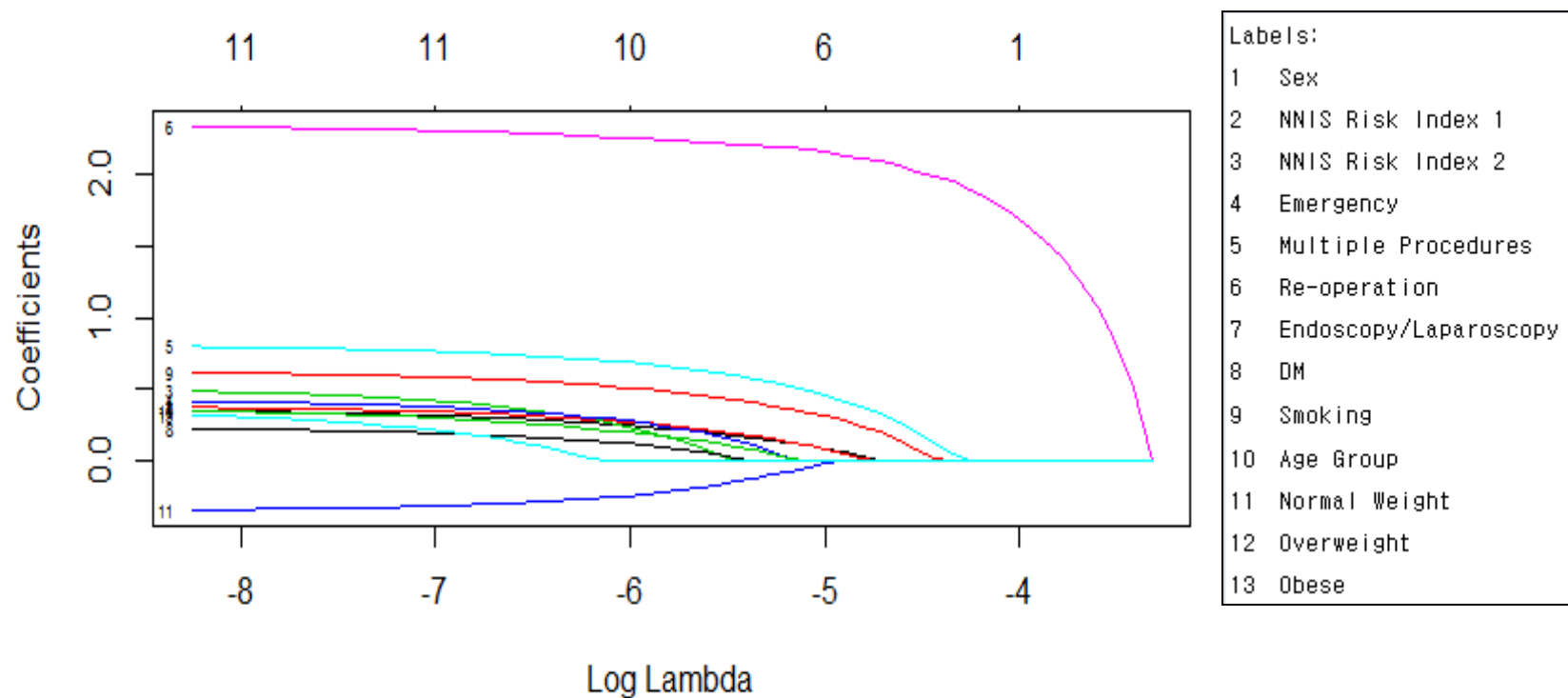


Figure 3.6. Lasso Coefficients on Model B as a Function of λ

Table 3.3. Estimate Beta Coefficients of Model A and Model B

| Variable | | Beta Coefficients | |
|--|-----------------------------|-------------------|------------------|
| | | Model A | Model B |
| (Intercept) | | -4.449904515 | -4.1264101 |
| Sex (Female vs Male) | | 0.186670666 | 0.3215283 |
| NNIS Risk Index | | | |
| | 0 | reference | reference |
| | 1 | 0.58140543 | 0.3480882 |
| | 2 | 0.695306453 | 0.4316985 |
| Emergency (No vs Yes) | | 0.023112765 | 0.384421 |
| Multiple Procedures in the Same Operation (No vs Yes) | | 0.795462202 | 0.7703042 |
| Re-operation (No vs Yes) | | 2.041290762 | 2.3144495 |
| Endoscopy/ Laparoscopy (No vs Yes) | | -0.001788328 | 0 |
| DM (No vs Yes) | | 0.155129297 | 0.198011 |
| Smoking (No vs Yes) | | 0.443936226 | 0.5895678 |
| Age Group (≤ 50 vs > 50) | | 0.555291627 | 0.3084608 |
| BMI | | | |
| Underweight | BMI < 18.5 | reference | reference |
| Normal | $18.5 \leq \text{BMI} < 25$ | -0.079223068 | -0.3215996 |
| Overweight | $25 \leq \text{BMI} < 30$ | 0.297702457 | 0 |
| Obese | BMI ≥ 30 | 0.50976252 | 0.2344054 |

Suppose the utilization of cross validation is to find lambda that gives the smallest MSE, such as

$$\lambda_A = 0.0006894738 \quad ; \quad \lambda_B = 0.000660882$$

or

$$\log(\lambda_A) = -7.279582 \quad ; \quad \log(\lambda_B) = -7.321935$$

which gave $\text{MSE}_A = 0.03548$ and $\text{MSE}_B = 0.03558$, however instead of using those lambda values, $\bar{\lambda}$ was used and gave kind of similar mean square error with $\text{MSE}_A = 0.03550$ and $\text{MSE}_B = 0.035584$.

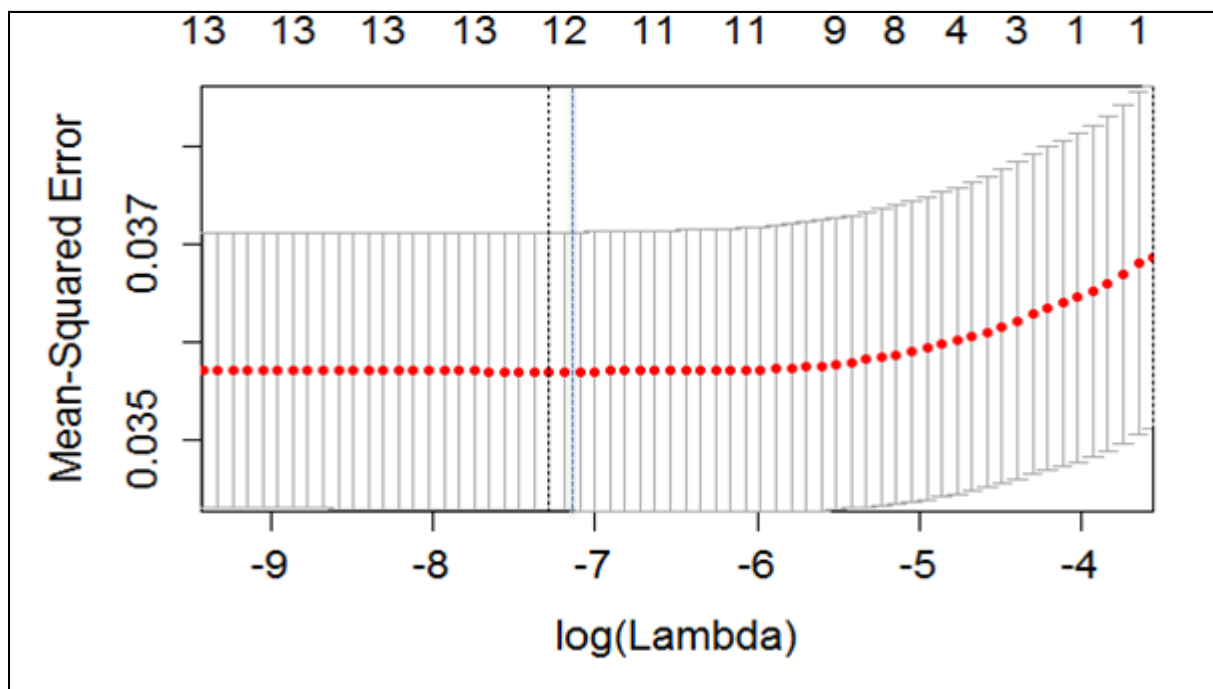


Figure 3.7. Cross-validation curve (red dotted line) of Model A with upper and lower standard deviation along the λ sequence (error bars)

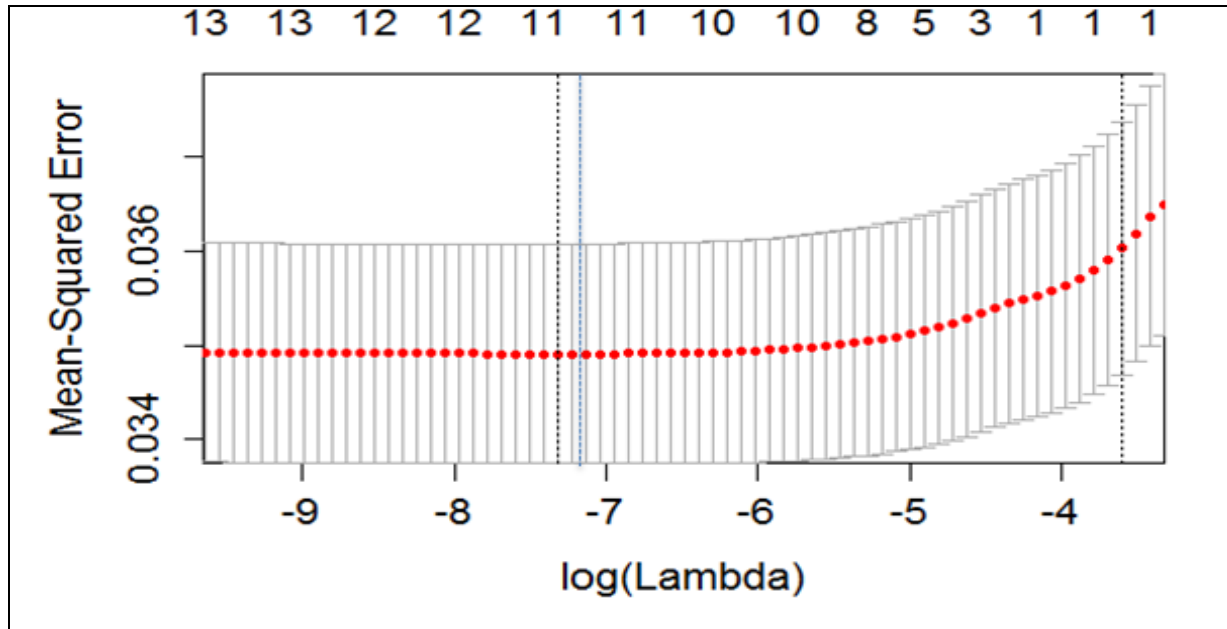


Figure 3.8. Cross-validation curve (red dotted line) of Model B with upper and lower standard deviation along the λ sequence (error bars)

In Figure 3.7 and 3.8; two selected λ are represented by the vertical dotted lines. Blue dotted line indicates $\bar{\lambda}$, while black dotted line after the blue one is λ_{\min} , the value of λ that gives minimum mean-cross validated error.

Once the candidates were obtained, forth, the performances of both models by re-fitting each estimate beta coefficients into testing set were compared. Based on the analysis, model B with AUC = 0.723, Hosmer-Lemeshow p-value = 0.398, and Brier Score = 0.03548 indicated better performance compared to model A; reciprocally, better calibration plot as well.

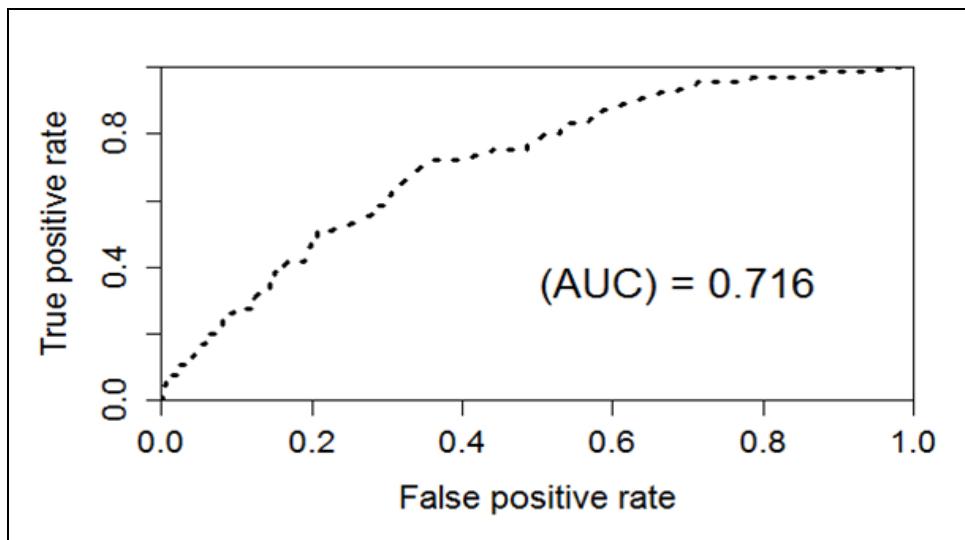


Figure 3.9. AUC of Model A Fitted on Testing Data Set

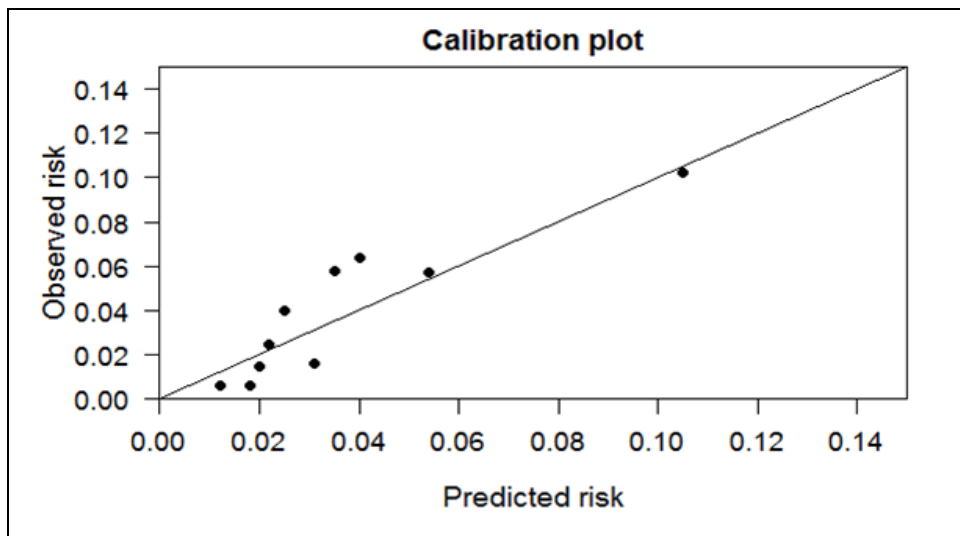


Figure 3.10. Calibration Plot of Model A Fitted on Testing Data Set

Table 3.4. Hosmer-Lemeshow Goodness of Fit Test of Model A (fitted on testing data set)

| | total | mean predicted | mean observed | predicted | observed |
|-----------------|--------------|---------------------------|--------------------------|------------------|-----------------|
| [0.0107,0.0135) | 178 | 0.012 | 0.006 | 2.08 | 1 |
| [0.0135,0.0186) | 170 | 0.018 | 0.006 | 3.02 | 1 |
| [0.0186,0.0222) | 203 | 0.02 | 0.015 | 4.14 | 3 |
| 0.0222 | 158 | 0.022 | 0.025 | 3.5 | 4 |
| [0.0222,0.0273) | 150 | 0.025 | 0.04 | 3.82 | 6 |
| [0.0273,0.0326) | 188 | 0.031 | 0.016 | 5.89 | 3 |
| [0.0326,0.0380) | 156 | 0.035 | 0.058 | 5.41 | 9 |
| [0.0380,0.0455) | 171 | 0.04 | 0.064 | 6.91 | 11 |
| [0.0455,0.0635) | 175 | 0.054 | 0.057 | 9.38 | 10 |
| [0.0635,0.4083] | 167 | 0.105 | 0.102 | 17.48 | 17 |
| Chi_square | df | p_value | | | |
| 10.141 | 8 | 0.2553 * | | | |

Note:* No evidence of poor fit

Unlike model A with Brier Score = 0.03550 where the value of AUC on the testing set was slightly lower (0.01 less than fitted on the training set), model B had the same AUC with c-statistics 0.723 (Figure 3.11). However, the calibration plot of model B was better when fitted on training set than on testing data set (Figure 3.12). Even so, approach Model B identified apparent relationships in the training data set that hold in general (minimal overfitting has been reduced).

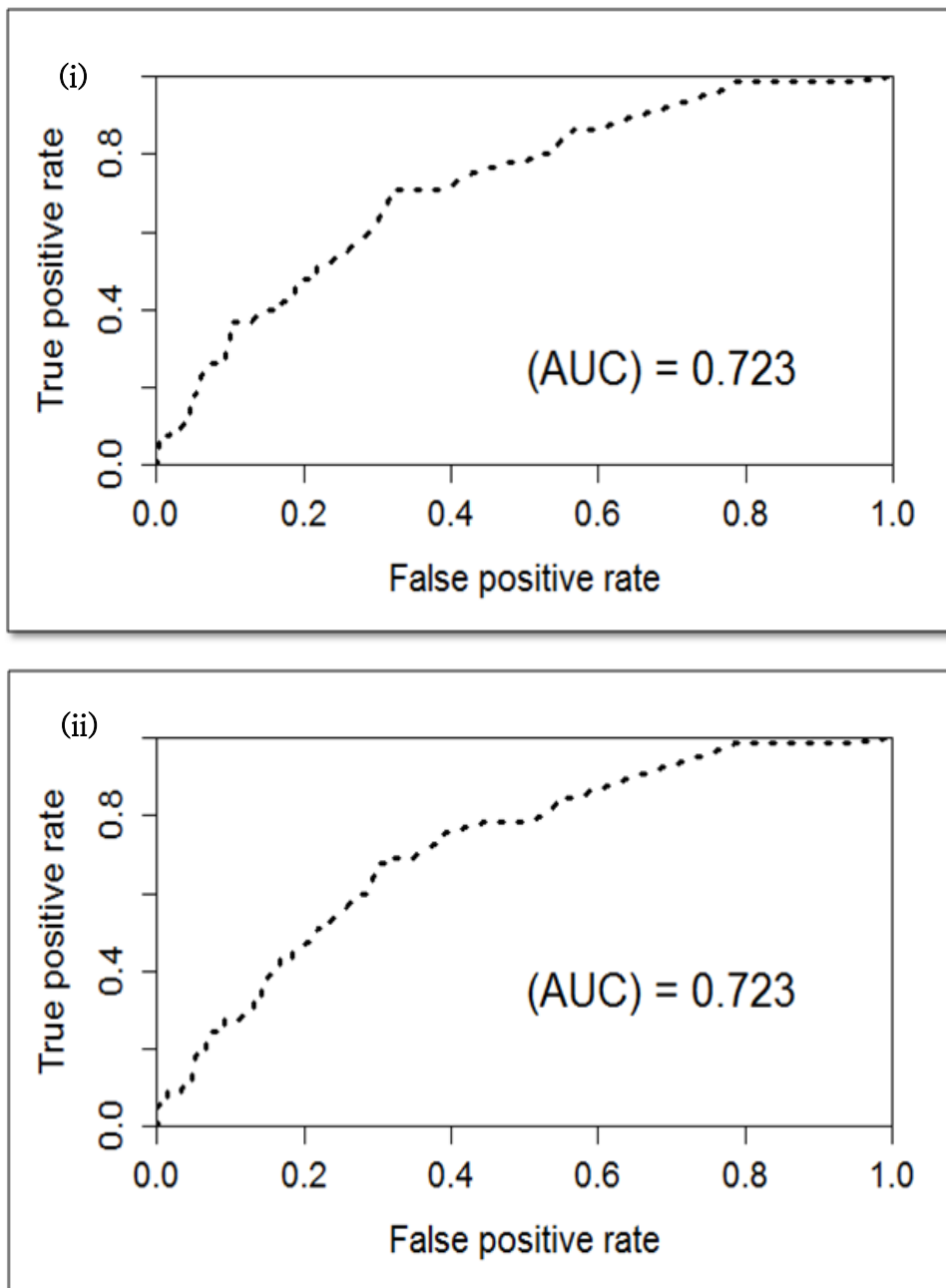


Figure 3.11. AUC of Model B: fitted on training (i) and testing set (ii)

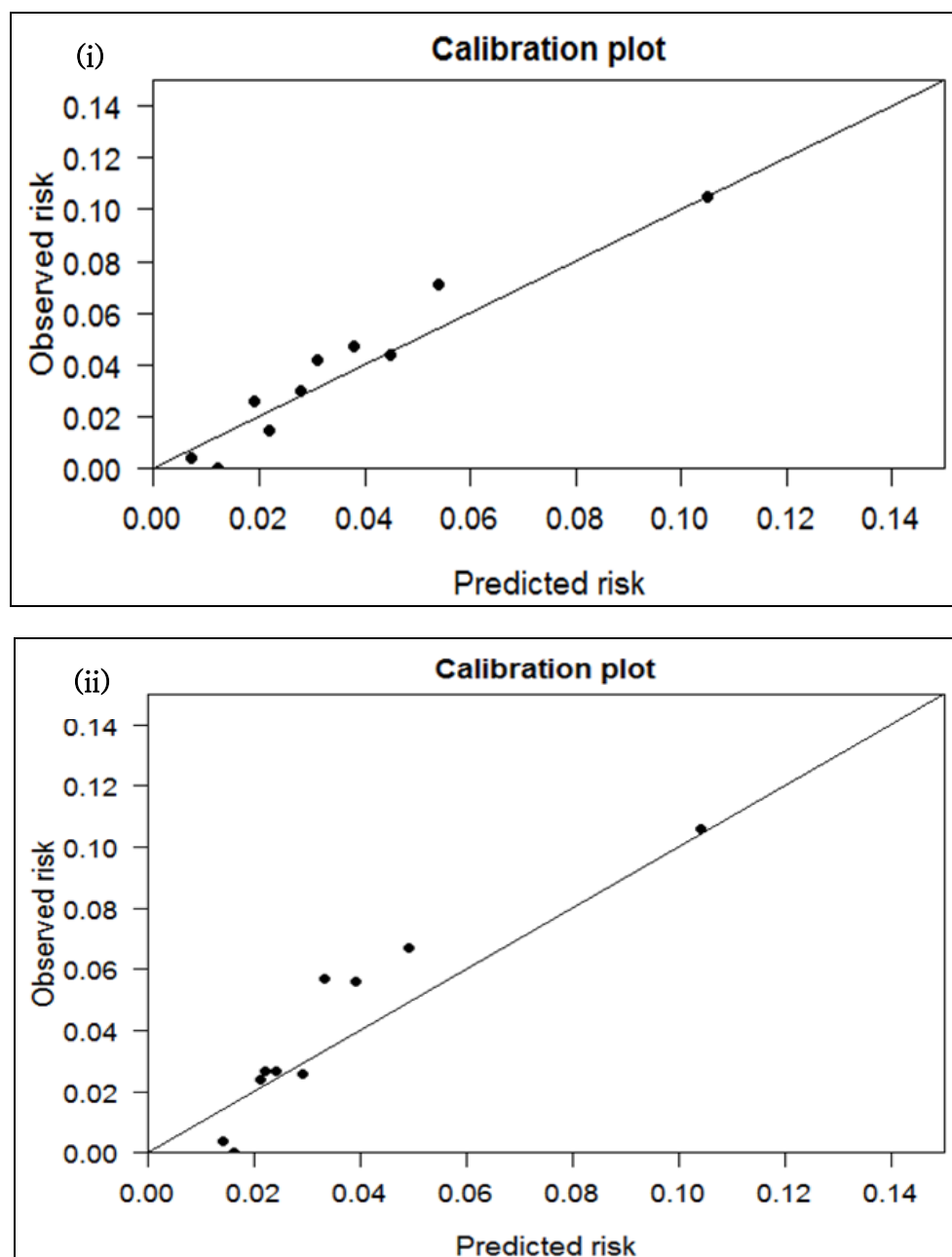


Figure 3.12. Calibration Plot of Model B: fitted on training (i) and testing set (ii)

Table 3.5. Hosmer-Lemeshow Goodness of Fit Test of Model B (fitted on testing data set)

| | total | mean predicted | mean observed | predicted | Observed |
|-----------------|-------|-------------------|------------------|-----------|----------|
| [0.0116,0.0159) | 229 | 0.014 | 0.004 | 3.21 | 1 |
| [0.0159,0.0190) | 127 | 0.016 | 0 | 2.03 | 0 |
| [0.0190,0.0215) | 247 | 0.021 | 0.024 | 5.25 | 6 |
| [0.0215,0.0221) | 113 | 0.022 | 0.027 | 2.44 | 3 |
| [0.0221,0.0274) | 149 | 0.024 | 0.027 | 3.62 | 4 |
| [0.0274,0.0302) | 233 | 0.029 | 0.026 | 6.84 | 6 |
| [0.0302,0.0365) | 106 | 0.033 | 0.057 | 3.53 | 6 |
| [0.0365,0.0421) | 179 | 0.039 | 0.056 | 6.98 | 10 |
| [0.0421,0.0538) | 163 | 0.049 | 0.067 | 7.97 | 11 |
| [0.0538,0.4755] | 170 | 0.104 | 0.106 | 17.71 | 18 |
| Chi_square | df | p_value | | | |
| 8.372 | 8 | 0.398 * | | | |

Note: * No evidence of poor fit

Thus, by lasso method, model B was chosen as the best model. Now let us compare between lasso and the existing method, stepwise logistic regression, to find out whether lasso is a good method to build risk prediction model. If used lasso, model A would not produce better performance than B, then by using stepwise logistic regression we obtained poor performance with AUC = 0.6950 (Figure 3.13) and Hosmer-Lemeshow P-value = 0.0356. Although model B showed slight better AUC with 0.6985 (Figure 3.14), yet model B also showed poor performance. Moreover, the indication of poor fit was shown by Hosmer-Lemeshow as well, with p-value <0.0001.

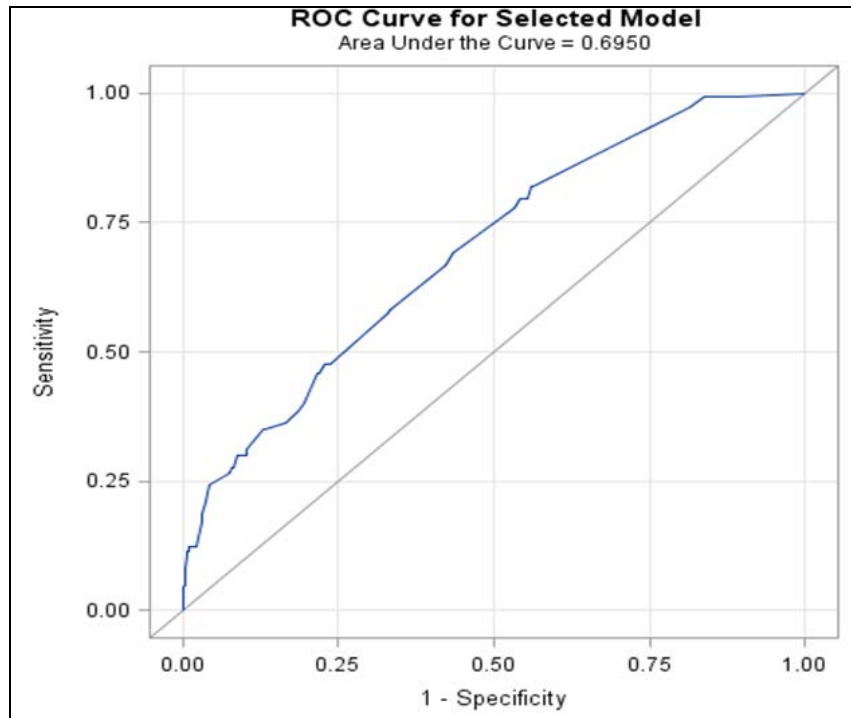


Figure 3.13. AUC of Model A by Stepwise Logistic Regression

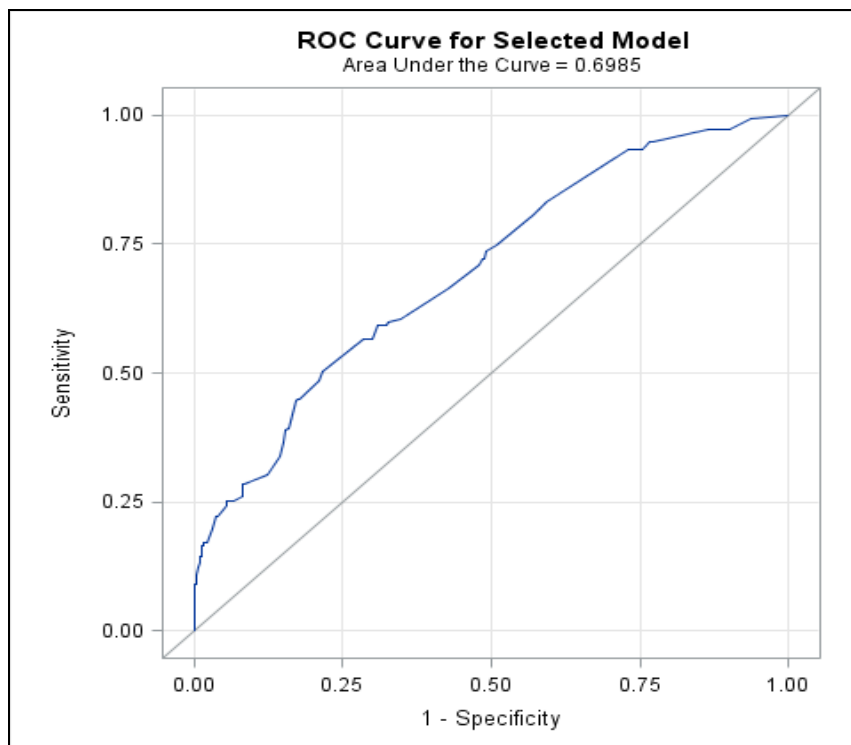


Figure 3.14. AUC of Model B by Stepwise Logistic Regression

It can be seen that lasso is indeed a good method, moreover, better than stepwise logistic regression. By lasso, model B was chosen as the best risk prediction model for gastric SSI with risk estimation of binary outcome (Y) for given value of factors (X_i) as follows:

$$P(Y | X_i) = \frac{1}{1 + e^{-(4.1264101 + \beta_i X_i)}} \quad (3.1)$$

Suppose every beta value corresponding to risk factors in Table 3.3 column model B is inserted into formula (3.1), then the estimate probability (risk) for each parameter can be seen in Table 3.6.

Table 3.6. Conversion table of lasso estimation to probability of getting infection after gastric surgery

| Host Factors: | | Estimate Coefficients | Estimate Risk |
|---|-----------------|-----------------------|---------------|
| Sex (male) | | 0.3215283 | 0.0218 |
| Age (> 50 years old) | | 0.3084608 | 0.0215 |
| Diabetes | | 0.198011 | 0.0193 |
| Smoking | | 0.5895678 | 0.0283 |
| BMI | | | |
| Underweight | BMI < 18.5 | reference | 0.0159 |
| Normal | 18.5 ≤ BMI < 25 | -0.3215996 | 0.0116 |
| Overweight | 25 ≤ BMI < 30 | 0 | 0.0159 |
| Obese | BMI ≥ 30 | 0.2344054 | 0.0200 |
| male + Age (>50) + DM + Smoking + Obesity | | | 0.0777 |
| Environmental / Treatment Factors: | | Estimate Coefficients | Estimate Risk |
| NNIS Risk Index | | | |
| | 0 | reference | 0.0159 |
| | 1 | 0.3480882 | 0.0224 |
| | 2 | 0.4316985 | 0.0243 |
| Emergency | | 0.384421 | 0.0232 |
| Multiple Procedures | | 0.7703042 | 0.0337 |
| Re-operation | | 2.3144495 | 0.1404 |
| NNIS Risk 2 + Emergency + Multiple Procedures + Re-operation | | | 0.4439 |

Based on Table 3.6, gastric SSI was more attributed to either environmental or treatment factors rather than to host factors. Among treatment factors, Re-operation at the same site was the variable which gave the highest risk of SSI (0.14). The risk itself was even greater than the estimate risk if all host factors were included (0.078).

After re-operation, multiple procedures was the parameter which gave the second highest risk of gastric SSI. The combination of re-operation and multiple procedures, when other factors that could increase the risk of SSI are not met, would give the estimate risk about 20%, obtained from

Define

No = 0

Yes = 1

$$\begin{aligned}
 &\Rightarrow P(Y_{SSI} = 1 | X_{re-operation} = 1, X_{multiple\ procedures} = 1, X_{BMI(normal)} = 1) \\
 &= \frac{1}{1 + \exp(-(-4.1264101 + 2.3144495(1) + 0.7703042(1) - 0.3215996(1)))} \\
 &= \frac{1}{1 + 3.908899982} = \frac{1}{4.908899982} \\
 &\approx 0.2037
 \end{aligned}$$

Suppose 0.33 is considered as the cutoff point to distinguish whether the patient has high risk of getting SSI or not. The risk estimation from simple combination of parameters where multiple procedures and re-operation set as fixed risk factors can be seen in Table 3.7.

Table 3.7. Estimate risk of gastric SSI by simple combination of risk factors in which multiple procedures and re-operation considered as fixed risk factors

| | | (Re-operation + Multiple Procedures) |
|--------------------------------|-----------------|--------------------------------------|
| Sex (male) | | 0.33 |
| Age (> 50 years old) | | 0.32 |
| Diabetes | | 0.30 |
| Smoking | | 0.39 |
| BMI | | 0.26 |
| Underweight | BMI < 18.5 | (Reference) 0.26 |
| Normal | 18.5 ≤ BMI < 25 | 0.20 |
| Overweight | 25 ≤ BMI < 30 | 0.26 |
| Obese | BMI ≥ 30 | 0.31 |
| NNIS Risk Index | | 0.31 |
| | 0 | (Reference) 0.26 |
| | 1 | 0.33 |
| | 2 | 0.35 |
| Emergency | | 0.34 |

Note: Cell with bold ink and grey highlight color are combination of variables classified as having high risk of infection post gastric surgery

Therefore, the minimum number of combinations of risk factors needed to classify as having high risk of gastric SSI is four parameters. As long as one of the five possible combinations are met,

1. male sex + under/overweight + re-operation + multiple procedures;
2. smoking + under/overweight + re-operation + multiple procedures;

3. NNIS risk index 1 + under/overweight + re-operation + multiple procedures;
4. NNIS risk index 2 + under/overweight + re-operation + multiple procedures; or
5. emergency + under/overweight + re-operation + multiple procedures

if the patient has other additional conditions, such as above 50 years old, having diabetes, or obesity, the risk of getting infected will even higher. The details combination of risk factors considered as having high risk of gastric SSI can be seen in Appendix Table 1.

IV. Discussion

The proposed risk prediction model for gastric surgical site infection was built based on Lasso problem. Instead of using ASA score, wound type, and T-hour variables; NNIS risk index was used as one of parameters that measured by those three equally weighted factors. Originally, NNIS risk index ranges from 0 to 3^[8-10, 12], however in this study, it ranged from 0 to 2 since NNIS risk index 3 was not found in the data were analyzed.

From 10 parameters; sex, NNIS risk index, emergency operative procedure, multiple procedures in the same operation, re-operation, diabetes, smoking, age, and BMI were statistically significant factors for gastric SSI. The findings were similar to several previously reported papers ^[13, 30-31]. While endoscopy/laparoscopy was shrunked towards 0, indicated that it was statistically insignificant risk factor associated with SSI after gastric surgery. Unlike reported in paper by Eiko Imai in 2008, laparoscopic gastric surgery was significant factor associated with lower SSI rate, approximately 75% less than that of open gastric surgery³¹. The difference may be occurred due to the samples size as well as the methodology as she used multivariate analysis.

Re-operation at the same site was found to be the factor that gave the largest risk to the incidence of gastric SSI with probability 0.140 or approximately 9 times higher risk than none re-operation;

followed by multiple procedures at the second place with probability 0.034. When these both criteria were met then the risk would increase sharply with probability about 0.20. Suppose the high risk SSI is defined as collection of risk factors with risk probability higher than or equal to 0.33, thus the presence of at least both re-operation and multiple procedures risk factors had become a kind of warning. Moreover, when other additional factors were combined with these two parameters, the resulting risk could be even higher, with value in the range of 0.20 - 0.81 (see Table 3.7 and Appendix Table 1).

In terms of BMI, compared to people with normal weight $18.5 \leq \text{BMI} < 25$, patient with either underweight, overweight, or obesity condition would have higher risk of getting infected post gastric surgery. Among these three conditions, patients with $\text{BMI} \geq 30$, or known as obesity, would be those with the highest risk of infection. In this study, both underweight and overweight conditions would give the same probability in terms of infection risk. Similar to the analysis conducted by Razavi in 2005, that even though BMI was failed proven as significant factor for abdominal SSI using chi-square test, however a trend in SSI rate was higher with low and high BMI¹⁶. It can be implied that the risk of gastric SSI by fine BMI categories have "U" shape curve and the risk is monotone increasing once the BMI larger than or equal to 25. Yet, we need further study to prove and validate this hypothesis since the findings may not be generalizable to all gastric SSI cases.

However this study has limitation, as there were only 7 patients with trauma but no indication of infection, thus the trauma variable was omitted, whereas trauma has been reported as one of significant factors for gastric SSI³⁰. We actually had sufficient data on trauma and might give much better model performance if the variable was included, but started from 2010, the whole data collection was not equipped with BMI, smoking, and DM variables. In addition, imputation was also not possible to handle the issues as the ratio in the number of missing data was much larger than that in non-missing data. Therefore, instead of reducing 3 parameters we cut the samples size by only using data from 2007 – 2009 which made trauma was omitted at the end due to irregularities beta value when included into the model.

In conclusion, this study presents that model building based on lasso problem is better than stepwise logistic regression and can produce a good and well calibrated risk prediction model on gastric SSI with c-statistic 0.723; 3.5 % higher compare to existing method with AUC only 0.6985. This study also shows that the emersion of gastric SSI is more affected by environmental/treatment factors, especially re-operation and multiple procedures, rather than host factors. Therefore, in order to minimize the risk, the surgeons are expected to be more careful in patient selection, preparation and medical care provision.

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Appendix

Appendix Table 1. Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|---|---|
| Male + Under/Overweight | 0.33 |
| NNIS Index Risk 1 + Age (>50) + Normal Weight | 0.33 |
| Male + NNIS Risk Index 1 + Normal Weight | 0.33 |
| NNIS Risk Index 1 + Under/Overweight | 0.33 |
| Male + Emergency + Normal Weight | 0.34 |
| Emergency + Under/Overweight | 0.34 |
| NNIS Index Risk 1 + Emergency + Normal Weight | 0.35 |
| NNIS Index Risk 2 + Age (>50) + Normal Weight | 0.35 |
| Male + NNIS Risk Index 2 + Normal Weight | 0.35 |
| NNIS Risk Index 2 + Under/Overweight | 0.35 |
| DM + Obesity | 0.35 |
| Smoking + DM + Normal Weight | 0.36 |
| NNIS Index Risk 2 + Emergency + Normal Weight | 0.37 |
| Male + Age (> 50) + DM + Normal Weight | 0.37 |
| Age (>50) + DM + Under/Overweight | 0.37 |
| Male + DM + Under/Overweight | 0.37 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|---|---|
| NNIS Risk Index 1 + Age (> 50) + DM + Normal Weight | 0.38 |
| Age (>50) + Obesity | 0.38 |
| Male + NNIS Risk Index 1 + DM + Normal Weight | 0.38 |
| NNIS Index Risk 1 + DM + Under/Overweight | 0.38 |
| Male + Obesity | 0.38 |
| Emergency + Age (> 50) + DM + Normal Weight | 0.38 |
| Smoking + Age (>50) + Normal Weight | 0.39 |
| NNIS Index Risk 1 + Obesity | 0.39 |
| Male + Smoking + Normal Weight | 0.39 |
| Smoking + Under/Overweight | 0.39 |
| NNIS Risk Index 1 + Emergency + DM + Normal Weight | 0.39 |
| Smoking + NNIS Risk Index 1 + Normal Weight | 0.40 |
| NNIS Risk Index 2 + Age (> 50) + DM + Normal Weight | 0.40 |
| Male + NNIS Risk Index 2 + DM + Normal Weight | 0.40 |
| NNIS Index Risk 2 + DM + Under/Overweight | 0.40 |
| Male + Age (> 50) + Under/Overweight | 0.40 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|--|---|
| Smoking + Emergency + Normal Weight | 0.40 |
| Male + NNIS Risk Index 1 + Age (>50) + Normal Weight | 0.40 |
| NNIS Index Risk 1 + Age (>50) + Under/Overweight | 0.40 |
| NNIS Index Risk 2 + Obesity | 0.41 |
| Male + NNIS Risk Index 1 + Under/Overweight | 0.41 |
| NNIS Risk Index 2 + Emergency + DM + Normal Weight | 0.41 |
| Smoking + NNIS Risk Index 2 + Normal Weight | 0.42 |
| Male + Emergency + Under/Overweight | 0.42 |
| NNIS Risk Index 1 + Emergency + Age (> 50) + Normal Weight | 0.42 |
| Male + NNIS Risk Index 1 + Emergency + Normal Weight | 0.42 |
| NNIS Index Risk 1 + Emergency + Under/Overweight | 0.42 |
| Male + NNIS Risk Index 2 + Age (>50) + Normal Weight | 0.43 |
| NNIS Index Risk 2 + Age (>50) + Under/Overweight | 0.43 |
| Age (> 50) + DM + Obesity | 0.43 |
| Male + NNIS Risk Index 2 + Under/Overweight | 0.43 |
| Male + DM + Obesity | 0.43 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|--|---|
| Smoking + Age (> 50) + DM + Normal Weight | 0.43 |
| NNIS Risk Index 1 + DM + Obesity | 0.44 |
| Male + Smoking + DM + Normal Weight | 0.44 |
| Smoking + DM + Under/Overweight | 0.44 |
| NNIS Risk Index 2 + Emergency + Age (> 50) + Normal Weight | 0.44 |
| Smoking + NNIS Risk Index 1 + DM + Normal Weight | 0.44 |
| Male + NNIS Risk Index 2 + Emergency + Normal Weight | 0.44 |
| NNIS Index Risk 2 + Emergency + Under/Overweight | 0.44 |
| Emergency + DM + Obesity | 0.44 |
| Smoking + Obesity | 0.45 |
| Male + Age (> 50) + DM + Under/Overweight | 0.45 |
| Male + NNIS Risk Index 1 + Age (>50) + DM + Normal Weight | 0.45 |
| NNIS Risk Index 1 + Age (> 50) + DM + Under/Overweight | 0.45 |
| NNIS Risk Index 2 + DM + Obesity | 0.46 |
| Male + Age (> 50) + Obesity | 0.46 |
| Male + NNIS Risk Index 1 + DM + Under/Overweight | 0.46 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation Multiple Procedures) + |
|--|---|
| Male + Emergency + Age (>50) + DM + Normal Weight | 0.46 |
| Emergency + Age (> 50) + DM + Under/Overweight | 0.46 |
| NNIS Risk Index 1 + Age (> 50) + Obesity | 0.46 |
| Smoking + NNIS Risk Index 2 + DM + Normal Weight | 0.46 |
| Male + Smoking + Age (>50) + Normal Weight | 0.46 |
| Smoking + Age (>50) + Under/Overweight | 0.46 |
| Male + NNIS Risk Index 1 + Obesity | 0.47 |
| Male + Smoking + Under/Overweight | 0.47 |
| Emergency + NNIS Risk Index 1 + Age (>50) + DM + Normal Weight | 0.47 |
| Smoking + NNIS Risk Index 1 + Age (>50) + Normal Weight | 0.47 |
| Emergency + Age (> 50) + Obesity | 0.47 |
| Male + NNIS Risk Index 1 + Emergency + DM + Normal Weight | 0.47 |
| NNIS Risk Index 1 + Emergency + DM + Under/Overweight | 0.47 |
| Male + Smoking + NNIS Risk Index 1 + Normal Weight | 0.47 |
| Smoking + NNIS Risk Index 1 + Under/Overweight | 0.47 |
| Male + NNIS Risk Index 2 + Age (>50) + DM + Normal Weight | 0.47 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation Multiple Procedures) + |
|--|---|
| NNIS Risk Index 2 + Age (> 50) + DM + Under/Overweight | 0.47 |
| Male + NNIS Risk Index 2 + DM + Under/Overweight | 0.48 |
| NNIS Risk Index 1 + Emergency + Obesity | 0.48 |
| Male + Smoking + Emergency + Normal Weight | 0.48 |
| Smoking + Emergency + Under/Overweight | 0.48 |
| NNIS Risk Index 2 + Age (> 50) + Obesity | 0.48 |
| Male + NNIS Risk Index 1 + Age (>50) + Under/Overweight | 0.48 |
| Male + NNIS Risk Index 2 + Obesity | 0.49 |
| Smoking + NNIS Risk Index 1 + Emergency + Normal Weight | 0.49 |
| Emergency + NNIS Risk Index 2 + Age (>50) + DM + Normal Weight | 0.49 |
| Smoking + NNIS Risk Index 2 + Age (>50) + Normal Weight | 0.49 |
| Male + NNIS Risk Index 2 + Emergency + DM + Normal Weight | 0.49 |
| NNIS Risk Index 2 + Emergency + DM + Under/Overweight | 0.49 |
| Male + Smoking + NNIS Risk Index 2 + Normal Weight | 0.49 |
| Smoking + NNIS Risk Index 2 + Under/Overweight | 0.49 |
| Smoking + DM + Obesity | 0.50 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation Multiple Procedures) + |
|--|---|
| Male + NNIS Risk Index 1 + Emergency + Age (>50) + Normal Weight | 0.50 |
| NNIS Risk Index 1 + Emergency + Age (> 50) + Under/Overweight | 0.50 |
| NNIS Risk Index 2 + Emergency + Obesity | 0.50 |
| Male + NNIS Risk Index 1 + Emergency + Under/Overweight | 0.50 |
| Male + NNIS Risk Index 2 + Age (>50) + Under/Overweight | 0.51 |
| Male + Age (>50) + DM + Obesity | 0.51 |
| Smoking + NNIS Risk Index 2 + Emergency + Normal Weight | 0.51 |
| NNIS Risk Index 1 + Age (>50) + DM + Obesity | 0.51 |
| Male + Smoking + Age (>50) + DM + Normal Weight | 0.51 |
| Smoking + Age (> 50) + DM + Under/Overweight | 0.51 |
| Male + NNIS Risk Index 1 + Obesity + DM | 0.52 |
| Male + Smoking + DM + Under/Overweight | 0.52 |
| Smoking + NNIS Risk Index 1 + Age (>50) + DM + Normal Weight | 0.52 |
| Male + NNIS Risk Index 2 + Emergency + Age (>50) + Normal Weight | 0.52 |
| NNIS Risk Index 2 + Emergency + Age (> 50) + Under/Overweight | 0.52 |
| Emergency + Age (>50) + DM + Obesity | 0.52 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation Multiple Procedures) + |
|--|---|
| Smoking + Age (> 50) + Obesity | 0.52 |
| Male + Smoking + NNIS Risk Index 1 + DM + Normal Weight | 0.52 |
| Smoking + NNIS Risk Index 1 + DM + Under/Overweight | 0.52 |
| Male + NNIS Risk Index 2 + Emergency + Under/Overweight | 0.52 |
| Male + Emergency + Obesity + DM | 0.52 |
| Male + Smoking + Obesity | 0.53 |
| Smoking + Emergency + Age (>50) + DM + Normal Weight | 0.53 |
| Emergency + NNIS Risk Index 1 + Obesity + DM | 0.53 |
| Male + Smoking + Emergency + DM + Normal Weight | 0.53 |
| Smoking + NNIS Risk Index 1 + Obesity | 0.53 |
| NNIS Risk Index 2 + Age (>50) + DM + Obesity | 0.53 |
| Male + NNIS Risk Index 1 + Age (>50) + DM + Under/Overweight | 0.53 |
| Male + NNIS Risk Index 2 + Obesity + DM | 0.54 |
| Smoking + NNIS Risk Index 1 + Emergency + DM + Normal Weight | 0.54 |
| Smoking + NNIS Risk Index 2 + Age (>50) + DM + Normal Weight | 0.54 |
| Male + Emergency + Age (>50) + DM + Under/Overweight | 0.54 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation Multiple Procedures) + |
|---|---|
| Male + NNIS Risk Index 1 + Age (>50) + Obesity | 0.54 |
| Male + Smoking + NNIS Risk Index 2 + DM + Normal Weight | 0.54 |
| Smoking + NNIS Risk Index 2 + DM + Under/Overweight | 0.54 |
| Male + Smoking + Age (>50) + Under/Overweight | 0.54 |
| Male + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Normal Weight | 0.55 |
| Emergency + NNIS Risk Index 1 + Age (>50) + DM + Under/Overweight | 0.55 |
| Male + Smoking + NNIS Risk Index 1 + Age (>50) + Normal Weight | 0.55 |
| Smoking + NNIS Risk Index 1 + Age (>50) + Under/Overweight | 0.55 |
| Emergency + NNIS Risk Index 2 + Obesity + DM | 0.55 |
| Male + Emergency + Age (>50) + Obesity | 0.55 |
| Male + NNIS Risk Index 1 + Emergency + DM + Under/Overweight | 0.55 |
| Smoking + NNIS Risk Index 2 + Obesity | 0.55 |
| Male + Smoking + NNIS Risk Index 1 + Under/Overweight | 0.55 |
| Male + NNIS Risk Index 2 + Age (>50) + DM + Under/Overweight | 0.55 |
| Emergency + NNIS Risk Index 1 + Age (>50) + Obesity | 0.56 |
| Smoking + NNIS Risk Index 2 + Emergency + DM + Normal Weight | 0.56 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|---|---|
| Male + Smoking + Emergency + Age (>50) + Normal Weight | 0.56 |
| Male + NNIS Risk Index 1 + Emergency + Obesity | 0.56 |
| Male + Smoking + Emergency + Under/Overweight | 0.56 |
| Male + NNIS Risk Index 2 + Age (>50) + Obesity | 0.56 |
| Smoking + NNIS Risk Index 1 + Emergency + Age (> 50) + Normal Weight | 0.57 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Normal Weight | 0.57 |
| Smoking + NNIS Risk Index 1 + Emergency + Under/Overweight | 0.57 |
| Male + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Normal Weight | 0.57 |
| Emergency + NNIS Risk Index 2 + Age (>50) + DM + Under/Overweight | 0.57 |
| Male + Smoking + NNIS Risk Index 2 + Age (>50) + Normal Weight | 0.57 |
| Smoking + NNIS Risk Index 2 + Age (>50) + Under/Overweight | 0.57 |
| Smoking + Age (>50) + DM + Obesity | 0.57 |
| Male + NNIS Risk Index 2 + Emergency + DM + Under/Overweight | 0.57 |
| Male + Smoking + NNIS Risk Index 2 + Under/Overweight | 0.57 |
| Male + Smoking + Obesity + DM | 0.57 |
| Emergency + NNIS Risk Index 2 + Age (>50) + Obesity | 0.58 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|--|---|
| Male + NNIS Risk Index 1 + Emergency + Age (>50) + Under/Overweight | 0.58 |
| Smoking + NNIS Risk Index 1 + Obesity + DM | 0.58 |
| Male + NNIS Risk Index 2 + Emergency + Obesity | 0.58 |
| Smoking + NNIS Risk Index 2 + Emergency + Age (> 50) + Normal Weight | 0.59 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Normal Weight | 0.59 |
| Smoking + NNIS Risk Index 2 + Emergency + Under/Overweight | 0.59 |
| Smoking + Emergency + Obesity + DM | 0.59 |
| Male + NNIS Risk Index 1 + Age (>50) + DM + Obesity | 0.59 |
| Male + Smoking + Age (>50) + DM + Under/Overweight | 0.59 |
| Male + Smoking + NNIS Risk Index 1 + Age (>50) + DM + Normal Weight | 0.60 |
| Smoking + NNIS Risk Index 1 + Age (>50) + DM + Under/Overweight | 0.60 |
| Male + NNIS Risk Index 2 + Emergency + Age (>50) + Under/Overweight | 0.60 |
| Male + Emergency + Age (>50) + DM + Obesity | 0.60 |
| Smoking + NNIS Risk Index 2 + Obesity + DM | 0.60 |
| Male + Smoking + Age (>50) + Obesity | 0.60 |
| Male + Smoking + NNIS Risk Index 1 + DM + Under/Overweight | 0.60 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|--|---|
| NNIS Risk Index 1 + Emergency + Age (>50) + DM + Obesity | 0.61 |
| Male + Smoking + Emergency + Age (>50) + DM + Normal Weight | 0.61 |
| Smoking + Emergency + Age (>50) + DM + Under/Overweight | 0.61 |
| Smoking + NNIS Risk Index 1 + Age (>50) + Obesity | 0.61 |
| Male + NNIS Risk Index 1 + Emergency + Obesity + DM | 0.61 |
| Male + Smoking + Emergency + DM + Under/Overweight | 0.61 |
| Male + Smoking + NNIS Risk Index 1 + Obesity | 0.61 |
| Male + NNIS Risk Index 2 + Age (>50) + DM + Obesity | 0.61 |
| Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Normal Weight | 0.61 |
| Smoking + Emergency + Age (>50) + Obesity | 0.62 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + DM + Normal Weight | 0.62 |
| Smoking + NNIS Risk Index 1 + Emergency + DM + Under/Overweight | 0.62 |
| Male + Smoking + NNIS Risk Index 2 + Age (>50) + DM + Normal Weight | 0.62 |
| Smoking + NNIS Risk Index 2 + Age (>50) + DM + Under/Overweight | 0.62 |
| Male + Smoking + Emergency + Obesity | 0.62 |
| Male + Smoking + NNIS Risk Index 2 + DM + Under/Overweight | 0.62 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|--|---|
| Smoking + NNIS Risk Index 1 + Emergency + Obesity | 0.63 |
| NNIS Risk Index 2 + Emergency + Age (>50) + DM + Obesity | 0.63 |
| Male + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Under/Overweight | 0.63 |
| Smoking + NNIS Risk Index 2 + Age (>50) + Obesity | 0.63 |
| Male + Smoking + NNIS Risk Index 1 + Age (>50) + Under/Overweight | 0.63 |
| Male + NNIS Risk Index 2 + Emergency + Obesity + DM | 0.63 |
| Male + Smoking + NNIS Risk Index 2 + Obesity | 0.63 |
| Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Normal Weight | 0.63 |
| Male + NNIS Risk Index 1 + Emergency + Age (>50) + Obesity | 0.64 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + DM + Normal Weight | 0.64 |
| Smoking + NNIS Risk Index 2 + Emergency + DM + Under/Overweight | 0.64 |
| Male + Smoking + Emergency + Age (>50) + Under/Overweight | 0.64 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + Normal Weight | 0.64 |
| Smoking + NNIS Risk Index 1 + Emergency + Age (> 50) + Under/Overweight | 0.64 |
| Smoking + NNIS Risk Index 2 + Emergency + Obesity | 0.65 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Under/Overweight | 0.65 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|--|---|
| Male + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Under/Overweight | 0.65 |
| Male + Smoking + NNIS Risk Index 2 + Age (>50) + Under/Overweight | 0.65 |
| Male + Smoking + Age (>50) + DM + Obesity | 0.65 |
| Smoking + NNIS Risk Index 1 + Age (>50) + DM + Obesity | 0.65 |
| Male + NNIS Risk Index 2 + Emergency + Age (>50) + Obesity | 0.65 |
| Male + Smoking + NNIS Risk Index 1 + Obesity + DM | 0.66 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + Normal Weight | 0.66 |
| Smoking + NNIS Risk Index 2 + Emergency + Age (> 50) + Under/Overweight | 0.66 |
| Smoking + Emergency + Age (>50) + DM + Obesity | 0.66 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Under/Overweight | 0.66 |
| Male + Smoking + Emergency + Obesity + DM | 0.67 |
| Smoking + NNIS Risk Index 1 + Emergency + Obesity + DM | 0.67 |
| Smoking + NNIS Risk Index 2 + Age (>50) + DM + Obesity | 0.67 |
| Male + Smoking + NNIS Risk Index 1 + Age (>50) + DM + Under/Overweight | 0.67 |
| Male + Smoking + NNIS Risk Index 2 + Obesity + DM | 0.68 |
| Male + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Obesity | 0.68 |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation Multiple Procedures) | + |
|---|---|----------|
| Male + Smoking + Emergency + Age (>50) + DM + Under/Overweight | 0.68 | |
| Male + Smoking + NNIS Risk Index 1 + Age (>50) + Obesity | 0.68 | |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Normal Weight | 0.69 | |
| Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Under/Overweight | 0.69 | |
| Smoking + NNIS Risk Index 2 + Emergency + Obesity + DM | 0.69 | |
| Male + Smoking + Emergency + Age (>50) + Obesity | 0.69 | |
| Male + Smoking + NNIS Risk Index 1 + Emergency + DM + Under/Overweight | 0.69 | |
| Male + Smoking + NNIS Risk Index 2 + Age (>50) + DM + Under/Overweight | 0.69 | |
| Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + Obesity | 0.69 | |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Obesity | 0.70 | |
| Male + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Obesity | 0.70 | |
| Male + Smoking + NNIS Risk Index 2 + Age (>50) + Obesity | 0.70 | |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Normal Weight | 0.70 | |
| Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Under/Overweight | 0.70 | |
| Male + Smoking + NNIS Risk Index 2 + Emergency + DM + Under/Overweight | 0.71 | |
| Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + Obesity | 0.71 | |

Appendix Table 1. (continue) Details combination of risk factors classified as having high probability of gastric SSI

| Risk Factors : | (Re-operation + Multiple Procedures) |
|--|---|
| Male + Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + Under/Overweight | 0.71 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Obesity | 0.72 |
| Male + Smoking + NNIS Risk Index 1 + Age (>50) + DM + Obesity | 0.72 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + Under/Overweight | 0.73 |
| Male + Smoking + Emergency + Age (>50) + DM + Obesity | 0.73 |
| Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Obesity | 0.74 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Obesity + DM | 0.74 |
| Male + Smoking + NNIS Risk Index 2 + Age (>50) + DM + Obesity | 0.74 |
| Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Obesity | 0.75 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Under/Overweight | 0.75 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Obesity + DM | 0.75 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + Obesity | 0.76 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Under/Overweight | 0.77 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + Obesity | 0.77 |
| Male + Smoking + NNIS Risk Index 1 + Emergency + Age (>50) + DM + Obesity | 0.79 |
| Male + Smoking + NNIS Risk Index 2 + Emergency + Age (>50) + DM + Obesity | 0.81 |

Abstract in Korean (국문초록)

위 수술 부위 감염에 위험 예측 모델

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배경: 수술부위감염은 수술 후에 일반적인 합병증으로 남아있다. 비록 대부분의 수술부위감염은 항생제로 치료되어져 왔지만 아직까지도 건강관련 삶의 질을 낮추고 재입원의 위험을 높이고 건강관리의 비용을 증가시켜 왔다. 그러므로 우리는 가능하면 그것의 유병율을 줄이거나 유지하는 방법을 찾을 필요가 있다. 이러한 전략이 실현되기 위해서는 역학을 이해하고 적절한 위험 요인들에 대해 외과의들에게 제공하는 것은 점점 필요하게 될 것이다.

목적: 위 수술을 받은 환자들에게서 위험인자 감염 병원균의 높은 위험을 가진 환자들을 정의하는 위험 예측 모델을 개발시킨다

방법: 2007년 7월부터 2009년 12월까지 위 수술을 받고 KONIS (Korean Nosocomial Infections Surveillance System)에 확실히 등록된 4290명의 환자들을 lasso 방법을 통해 수술부위감염의 발생을 예측하였다. 교차검증은 lasso 과정 중에 사용되는 tuning parameter를 얻기 위해 사용되었다.

결과: 위 수술후나이,성별, NNIS Risk Index, 같은 수술에서 다중 절차, 같은 부위에 재수술,위급성, BMI, 당뇨, 현재 흡연여부 등이 통계적으로 유의한 요인들로 나타났다.그 요인들 중에 재수술이 확률은 0.14로 재수술을 안한 것보다 8.8 배 위험성이 높아 수술부위감염의 발생에 가장 크게 기여하고 있었다.그리고 그 다음은 수술시 다중 절차로 확률이 0.034로 나왔다.만약 높은 위험성이 0.33 보다 크거나 같은 확률로 정의될경우 위 두가지 요인들이 만족시킬 때 그 위험성에 대한 확률은 약 0.2 정도로 늘어난다.또한 다른 추가적인 요인들이 결합되었을 때0.2 에서 0.81 의 범위를 보이면서 그 위험성은 더 올라간다 BMI 의 경우18,5 보다 작거나 25에서 30 사이의 수치를 가진 환자들에게서는 유의한 차이를 보이지 않았지만 30 이상의 BMI를 가진 환자들에게서는 체중이 적거나 과체중인 사람들에 비해 25 % 정도 위험성이 높았다.

결론: lasso를 기반으로 한 모델은 stepwise logistic regression보다더 낮고,위 수술부위의 감염에 대한 잘 보정된 위험예측모델을만들수 있다. 이 연구는 또한 위수술부위감염에 있어서 숙주 요인들보다 재수술이나 수술시 다중절차들과 같은 환경적인 요인들이 더 영향을 미친다는 것을 보여주고 있다.그러므로 외과의들은 환자선별, 준비,의료적 주의 규정에 더 신경 쓸 필요가 있다.

주요어: 수술부위감염,위수술, KONIS, lasso, 교차 검증

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